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# QSAR Studies of Di/Triorganotin(IV) Complexes of Schiff Bases Derived from 2-Benzoyl Pyridine and Substituted Benzoic Acid Hydrazides

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Quantitative structure activity relationship (QSAR) analysis for the *in vitro* antimicrobial activity and structural descriptors coding for various molecular properties of di/triorganotin(IV) complexes of Schiff bases derived from 2-benzoyl pyridine and 2-and 4-substituted benzoic acid hydrazides and their di/triorganotin(IV) complexes have been studied. The QSAR results divulges the role of molecular connectivity indices, kappa shape indices, energy of lowest unoccupied molecular orbital and dipole moment in control and moderation of antibacterial and antifungal activity of the synthesized complexes. The observed and predicted antibacterial activity close to each other as they have got low residual values which supports the fact that that QSAR model is valid one and reliable for prediction of antibacterial activity.

**Keywords: QSAR, Antimicrobial activity, Di/Triorganotin(IV) complexes.**

## INTRODUCTION

Now a days, new safer antimicrobial drugs have been synthesized incredibly as the persistant microorganisms are developing resistance towards conventional drugs [1]. In recent years wide studies have been made on nitrogen containing Schiff bases due to their prominent pharmacological applications [2]. The Schiff bases with their metal complexes have revealed significant biological activity [3]. These compounds displayed a number of pharmacological applications such as antimicrobial [4], anticonvulsant [5], anti-inflammatory [6], anticancer [7], antituberclosis [8] agents. Further, these compounds are found to be potent antiproliferative agents mainly against leukemia and neuroblastoma, as these compounds become more carcinostatic on complexation. The organotin compounds are served as potent scaffolds as catalysts, surface disinfectants, light emitting diodes antifouling agent in material protection, wood preservatives, PVC stabilizers as well as non-linear optics *etc*. The bioactivity of the metal complexes enhanced on complexation when compared to the ligands due to its ability to diminish DNA of the microbes. It is not easy to discover biochemical pharmacological and toxicological endpoints. The quantitative structure-activity relationship (QSAR) modeling of the biological activity of the compounds is a very vital tool to evaluate and predict the activity of compounds against a therapeutic target. QSAR was carried out to correlate antimicrobial activity of synthesized compounds with their molecular descriptors using the linear free energy relationship model.

## EXPERIMENTAL

The molecular mechanics force field (MM) process of Hyperchem 6.03 was used for the pre-optimization of the structures of test compounds and the resulting geometries were further refined by means of the semiempirical method PM3 (Parametric Method-3). A gradient norm limit of 0.01 kcal/Å was used for the geometry optimization. The minimum energy structure of each molecule was used for the calculation of physico-chemical parameters using TSAR 3.3 software for Windows. The regression analysis was done by using the SPSS software package. Predictive power and model's corpulence were assessed by means of cross-validation coefficient $q^2_{LOO}$ (leave one out) method in which a model is developed by n-1 compounds and the $n^{th}$ compound is predicted. The model with

high $q^2_{LOO}$ value is considered to have high predictive ability. It is the only method that makes use of all the information on hand and is very relevant.

## RESULTS AND DISCUSSION

The synthesis, characterization and antimicrobial activity of di/triorganotin(IV) complexes of Schiff bases of benzoylpyridine derived hydrazones have been reported earlier. The MIC values of all the compounds has been shown in Table-1. In continuation of our research work, QSAR studies of the earlier synthesized compounds have been presented in this paper. QSAR analysis for the *in vitro* antimicrobial activity and structural descriptors coding for various molecular properties of di/triorganotin(IV) complexes of Schiff bases have been carried out to find the mathematical relationship between alteration in structure and antimicrobial activity using the linear free energy relationship model (LFER) described by Hansch and Fujita [9]. The dependent variable pMIC (*i.e.* -log MIC, Table-2) used as in QSAR study was obtained by taking negative logarithm of observed antimicrobial activity (*i.e.* MIC). The structural descriptors Kier's zero, first, second and third order molecular connectivity ($^0\chi$, $^0\chi^v$, $^1\chi$, $^1\chi^v$, $^2\chi$, $^2\chi^v$, $^3\chi$, $^3\chi^v$) and kappa shape ($\kappa_1$, $\kappa_2$, $\kappa_3$, $\kappa\alpha_1$, $\kappa\alpha_2$, $\kappa\alpha_3$) topological indices, Randic topological index (R), Balaban topological index (J), Wiener topological index (W), Total energy ($T_e$), energies of highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO), dipole moment ($\mu$), nuclear repulsion energy (Nu.E) and electronic energy (Ele.E), calculated for di/triorganotin(IV) complexes [10-15].

The preliminary regression analysis pointed out six compounds *viz.* 2, 5, 11, 13, 19 and 20 which have their resultant values outside the experimental limits and these were not included for generation of QSAR models for further studies. The interaction between molecular descriptors and antimicrobial activity was analyzed on the basis of regression analysis and correlation matrix constructed for antibacterial activity against *Escherichia coli* is presented in Table-3. The interrelationship between different structural descriptors and antimicrobial activities is presented in Table-4. A general overview of the whole data set indicated high co-linearity ($r > 0.8$) between different parameters *i.e.* molecular descriptors. The high interrelationship was observed between first order molecular connectivity index ($^0\chi$) and Randic parameter (R), ($r = 1.000$), zero order molecular connectivity index, $^0\chi$ and electronic energy, Ele.E ($r = 0.998$), nuclear repulsion energy, NuE and zero order molecular connectivity index, $^0\chi$ ($r = 0.998$) and lowest correlation was observed between third order molecular connectivity index, $^3\chi$ and first order molecular connectivity index, $^1\chi$ ($r = 0.005$) and third order molecular connectivity index, $^3\chi$ and Randic parameter, R ($r = 0.005$). The correlation matrix indicated the role of molecular connectivity indices, kappa shape indices, energy of lowest unoccupied molecular

TABLE-1
*in vitro* ANTIMICROBIAL ACTIVITY OF SCHIFF BASES DERIVED FROM 2-BENZOYL PYRIDINE WITH 2- AND 4-SUBSTITUTED BENZOIC ACID HYDRAZIDES AND THEIR DI/TRIORGANOTIN(IV) COMPLEXES

| Compounds | Minimum inhibitory concentration (MIC, μM/mL) | | | | | |
|---|---|---|---|---|---|---|
| | Gram-negative bacteria | | Gram-positive bacteria | | Fungi | |
| | *E. coli* | *P. aeruginosa* | *B. cereus* | *S. aureus* | *A. niger* | *A. flavus* |
| $H_1L^1$ | 0.0361 | 0.0361 | 0.0361 | 0.0180 | 0.0090 | 0.0180 |
| $H_1L^2$ | 0.0361 | 0.0361 | 0.0361 | 0.0180 | 0.0090 | 0.0180 |
| $H_1L^3$ | 0.0396 | 0.0396 | 0.0396 | 0.0198 | 0.0198 | 0.0198 |
| $H_1L^4$ | 0.0372 | 0.0186 | 0.0186 | 0.0186 | 0.0186 | 0.0093 |
| $Ph_2SnL^1Cl$ (1) | 0.0096 | 0.0096 | 0.0191 | 0.0096 | 0.0048 | 0.0024 |
| $Bu_2SnL^1Cl$ (2) | 0.0102 | 0.0051 | 0.0051 | 0.0025 | 0.0051 | 0.0025 |
| $Me_2SnL^1Cl$ (3) | 0.0236 | 0.0059 | 0.0118 | 0.0118 | 0.0059 | 0.0059 |
| $Ph_3SnL^1$ (4) | 0.0090 | 0.0045 | 0.0090 | 0.0090 | 0.0090 | 0.0045 |
| $Bu_3SnL^1$ (5) | 0.0197 | 0.0098 | 0.0098 | 0.0098 | 0.0098 | 0.0049 |
| $Me_3SnL^1$ (6) | 0.0246 | 0.0123 | 0.0246 | 0.0123 | 0.0123 | 0.0061 |
| $Ph_2SnL^2Cl$ (7) | 0.0096 | 0.0048 | 0.0048 | 0.0024 | 0.0024 | 0.0048 |
| $Bu_2SnL^2Cl$ (8) | 0.0204 | 0.0051 | 0.0102 | 0.0051 | 0.0025 | 0.0051 |
| $Me_2SnL^2Cl$ (9) | 0.0236 | 0.0059 | 0.0118 | 0.0029 | 0.0059 | 0.0059 |
| $Ph_3SnL^2$ (10) | 0.0090 | 0.0090 | 0.0090 | 0.0045 | 0.0045 | 0.0045 |
| $Bu_3SnL^2$ (11) | 0.0197 | 0.0098 | 0.0098 | 0.0098 | 0.0025 | 0.0049 |
| $Me_3SnL^2$ (12) | 0.0246 | 0.0123 | 0.0123 | 0.0123 | 0.0061 | 0.0061 |
| $Ph_2SnL^3Cl$ (13) | 0.0100 | 0.0050 | 0.0100 | 0.0025 | 0.0025 | 0.0025 |
| $Bu_2SnL^3Cl$ (14) | 0.0215 | 0.0054 | 0.0107 | 0.0107 | 0.0107 | 0.0054 |
| $Me_2SnL^3Cl$(15) | 0.0251 | 0.0125 | 0.0125 | 0.0031 | 0.0031 | 0.0031 |
| $Ph_3SnL^3$ (16) | 0.0094 | 0.0094 | 0.0094 | 0.0049 | 0.0049 | 0.0049 |
| $Bu_3SnL^3$ (17) | 0.0207 | 0.0103 | 0.0207 | 0.0103 | 0.0103 | 0.0052 |
| $Me_3SnL^3$ (18) | 0.0261 | 0.0131 | 0.0131 | 0.0131 | 0.0131 | 0.0065 |
| $Ph_2SnL^4Cl$ (19) | 0.0097 | 0.0097 | 0.0097 | 0.0024 | 0.0024 | 0.0024 |
| $Bu_2SnL^4Cl$ (20) | 0.0104 | 0.0052 | 0.0104 | 0.0052 | 0.0104 | 0.0052 |
| $Me_2SnL^4Cl$(21) | 0.0241 | 0.0120 | 0.0120 | 0.0060 | 0.0120 | 0.0060 |
| $Ph_3SnL^4$ (22) | 0.0091 | 0.0091 | 0.0046 | 0.0046 | 0.0046 | 0.0046 |
| $Bu_3SnL^4$ (23) | 0.0200 | 0.0100 | 0.0100 | 0.0100 | 0.0100 | 0.0100 |
| $Me_3SnL^4$ (24) | 0.0251 | 0.0125 | 0.0125 | 0.0125 | 0.0125 | 0.0063 |
| Ciprofloxacin | 0.0047 | 0.0047 | 0.0047 | 0.0047 | – | – |
| Fluconazole | – | – | – | – | 0.0102 | 0.0102 |

TABLE-2
pMIC VALUES OF *in vitro* ANTIMICROBIAL ACTIVITY OF SCHIFF BASES DERIVED FROM 2-BENZOYL PYRIDINE WITH 2- AND 4-SUBSTITUTED BENZOIC ACID HYDRAZIDES AND THEIR DI/TRIORGANOTIN (IV) COMPLEXES

| Compd. | pMICec | pMICpa | pMICbc | pMICsa | pMICan | pMICaf |
|---|---|---|---|---|---|---|
| $H_1L^1$ | 1.442 | 1.442 | 1.442 | 1.745 | 2.046 | 1.745 |
| $H_1L^2$ | 1.442 | 1.442 | 1.442 | 1.745 | 2.046 | 1.745 |
| $H_1L^3$ | 1.402 | 1.402 | 1.402 | 1.703 | 1.703 | 1.703 |
| $H_1L^4$ | 1.429 | 1.730 | 1.730 | 1.730 | 1.730 | 2.032 |
| 1 | 2.018 | 2.018 | 1.719 | 2.018 | 2.319 | 2.620 |
| 2 | 1.991 | 2.292 | 2.292 | 2.602 | 2.292 | 2.602 |
| 3 | 1.627 | 2.229 | 1.928 | 1.928 | 2.229 | 2.229 |
| 4 | 2.046 | 2.347 | 2.046 | 2.046 | 2.046 | 2.347 |
| 5 | 1.706 | 2.009 | 2.009 | 2.009 | 2.009 | 2.310 |
| 6 | 1.609 | 1.910 | 1.609 | 1.910 | 1.910 | 2.215 |
| 7 | 2.018 | 2.319 | 2.319 | 2.620 | 2.620 | 2.319 |
| 8 | 1.690 | 2.292 | 1.991 | 2.292 | 2.602 | 2.292 |
| 9 | 1.627 | 2.229 | 1.928 | 2.538 | 2.229 | 2.229 |
| 10 | 2.046 | 2.046 | 2.046 | 2.347 | 2.347 | 2.347 |
| 11 | 1.706 | 2.009 | 2.009 | 2.009 | 2.602 | 2.310 |
| 12 | 1.609 | 1.910 | 1.910 | 1.910 | 2.215 | 2.215 |
| 13 | 2.000 | 2.301 | 2.000 | 2.602 | 2.602 | 2.602 |
| 14 | 1.668 | 2.268 | 1.971 | 1.971 | 1.971 | 2.268 |
| 15 | 1.600 | 1.903 | 1.903 | 2.509 | 2.509 | 2.509 |
| 16 | 2.027 | 2.027 | 2.027 | 2.310 | 2.310 | 2.310 |
| 17 | 1.684 | 1.987 | 1.684 | 1.987 | 1.987 | 2.284 |
| 18 | 1.583 | 1.883 | 1.883 | 1.883 | 1.883 | 2.187 |
| 19 | 2.013 | 2.013 | 2.013 | 2.620 | 2.620 | 2.620 |
| 20 | 1.983 | 2.284 | 1.983 | 2.284 | 1.983 | 2.284 |
| 21 | 1.618 | 1.921 | 1.921 | 2.222 | 1.921 | 2.222 |
| 22 | 2.041 | 2.041 | 2.337 | 2.337 | 2.337 | 2.337 |
| 23 | 1.699 | 2.000 | 2.000 | 2.000 | 2.000 | 2.000 |
| 24 | 1.600 | 1.903 | 1.903 | 1.903 | 1.903 | 2.201 |
| Std. | 2.610 | 2.610 | 2.610 | 2.610 | 2.610 | 2.610 |

orbital and dipole moment in control and moderation of antibacterial and antifungal activity of the synthesized complexes.

The computational studies revealed the importance of second order molecular connectivity index ($^2\chi$) in modulating the antibacterial potential of synthesized compounds against *E. coli* and the developed QSAR model is represented by eqn. 1. Topological indices are numerical quantifiers of molecular topology and are sensitive to bonding pattern, symmetry, content of heteroatom as well as degree of complexity of atomic neighbourhoods. The second order molecular connectivity topological index ($^2\chi$) represents the molecules with branched structure [16,17].

**QSAR model for antibacterial activity against *E. coli***

$$pMIC_{ec} = 0.0697\ ^2\chi + 0.637 \quad (1)$$

$n = 22, r = 0.958, r^2 = 0.917, q^2 = 0.898, s = 0.065, F = 221.349$

Here and thereafter, n - number of data points, r - correlation coefficient, $r^2$ - squared correlation coefficient, $q^2$ - cross validated $r^2$ obtained by leave one out method, s - standard error of the estimate and F - Fischer statistics.

**QSAR model for antibacterial activity against *E. coli***

$$pMIC_{ecMLR} = 0.073\ ^2\chi - 0.0048\ ^3\chi^v + 0.660 \quad (2)$$

$n = 22, r = 0.978, r^2 = 0.945, q^2 = 0.945, s = 0.049, F = 20.852$

The eqn. 1 represents monoparametric QSAR model (Linear regression, LR) with r value 0.958 and an attempt was made to enhance the r value in order to increase the predictability and reliability of derived QSAR model, which resulted in an another biparametric QSAR model (multiple linear regression, MLR) [18,19], which was obtained by inclusion of valence third order molecular connectivity index $^3\chi^v$ along with second order molecular connectivity index as a determinant factor (eqn. 2). The r value was increased from 0.958 to 0.978 and $q^2$ value rose to 0.945 from 0.898 in eqn. 2 and eqn. 1, respec-tively. Also the QSAR model represented by eqn. 2 has got $r^2$ value 0.945 which indicated that this model can correctly predict the antibacterial activity of approximately 94.5 % compounds of similar structures. The statistical validity of derived QSAR models was assessed by leave one out method, according to which a model should have $q^2$ values ≥ 0.5, to be considered as valid and both the models (eqns. 1 and 2) have got high $q^2$ values. The biparametric model (eqn. 2) was considered for the prediction of antibacterial activity against *E. coli* and the results presented in Table-5 indicated that the observed and predicted antibacterial activity lie close to each other as they have got low residual values which supports the fact that that QSAR model represented by eqn. 2 is valid one and reliable for prediction of antibacterial activity.

TABLE-3
CORRELATION MATRIX OF STRUCTURAL DESCTRIPTORS FOR SCHIFF BASES DERIVED FROM 2-BENZOYL PYRIDINE WITH 2-AND 4-SuBSTITUTED BENZOIC ACID HYDRAZIDES AND THEIR DI/TRIORGANOTIN(IV) COMPLEXES FOR ANTIMICROBIAL ACTIVITY AGAINST *E. coli*

| | $^0\chi$ | $^0\chi^v$ | $^1\chi$ | $^1\chi^v$ | $^2\chi$ | $^2\chi^v$ | $^3\chi$ | $^3\chi^v$ | $\kappa_1$ | $\kappa_2$ | R | Te | Ele.E | NuE | LUMO | μ | $pMIC_{ec}$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $^0\chi$ | 1.000 | | | | | | | | | | | | | | | | |
| $^0\chi^v$ | 0.936 | 1.000 | | | | | | | | | | | | | | | |
| $^1\chi$ | 0.994 | 0.906 | 1.000 | | | | | | | | | | | | | | |
| $^1\chi^v$ | 0.624 | 0.835 | 0.552 | 1.000 | | | | | | | | | | | | | |
| $^2\chi$ | 0.953 | 0.949 | 0.933 | 0.777 | 1.000 | | | | | | | | | | | | |
| $^2\chi^v$ | 0.425 | 0.679 | 0.344 | 0.970 | 0.626 | 1.000 | | | | | | | | | | | |
| $^3\chi$ | 0.088 | 0.349 | 0.005 | 0.798 | 0.356 | 0.914 | 1.000 | | | | | | | | | | |
| $^3\chi^v$ | -0.049 | 0.236 | -0.133 | 0.729 | 0.217 | 0.872 | 0.983 | 1.000 | | | | | | | | | |
| $\kappa_1$ | 0.987 | 0.895 | 0.987 | 0.524 | 0.891 | 0.308 | -0.051 | -0.181 | 1.000 | | | | | | | | |
| $\kappa_2$ | 0.674 | 0.439 | 0.723 | -0.117 | 0.431 | -0.349 | -0.665 | -0.752 | 0.776 | 1.000 | | | | | | | |
| R | 0.994 | 0.906 | 1.000 | 0.552 | 0.933 | 0.344 | 0.005 | -0.133 | 0.987 | 0.723 | 1.000 | | | | | | |
| Te | -0.984 | -0.910 | -0.970 | -0.628 | -0.947 | -0.442 | -0.127 | 0.006 | -0.967 | -0.642 | -0.970 | 1.000 | | | | | |
| Ele.E | -0.998 | -0.937 | -0.992 | -0.619 | -0.943 | -0.418 | -0.073 | 0.060 | -0.989 | -0.685 | -0.992 | 0.980 | 1.000 | | | | |
| NuE | 0.998 | 0.938 | 0.992 | 0.618 | 0.942 | 0.416 | 0.070 | -0.063 | 0.989 | 0.687 | 0.992 | -0.977 | -1.000 | 1.000 | | | |
| LUMO | -0.236 | -0.166 | -0.198 | -0.229 | -0.285 | -0.237 | -0.239 | -0.223 | -0.211 | -0.036 | -0.198 | 0.379 | 0.213 | -0.201 | 1.000 | | |
| μ | 0.124 | 0.152 | 0.069 | 0.336 | 0.221 | 0.382 | 0.422 | 0.414 | 0.078 | -0.183 | 0.069 | -0.251 | -0.093 | 0.082 | -0.802 | 1.000 | |
| pMICec | 0.943 | 0.871 | 0.949 | 0.607 | 0.958 | 0.433 | 0.157 | 0.016 | 0.894 | 0.548 | 0.949 | -0.936 | -0.933 | 0.932 | -0.264 | 0.144 | 1.000 |

TABLE-4
MOLECULAR DESCRIPTORS FOR SCHIFF BASES DERIVED FROM 2-BENZOYL PYRIDINE WITH 2- AND 4-SUBSTITUTED BENZOIC ACID HYDRAZIDES AND THEIR DI/TRIORGANOTIN(IV) COMPLEXES

| Comp. | $^1\chi$ | $^1\chi^v$ | $^2\chi$ | $^2\chi^v$ | $^3\chi$ | $^3\chi^v$ | $\kappa_1$ | $\kappa_2$ | $\kappa_3$ | R | J | W | Te | Ele.E | NuE | LUMO | HOMO | M |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $H_1L^1$ | 12.66 | 7.75 | 10.87 | 5.26 | 1.31 | 0.43 | 20.73 | 10.52 | 5.75 | 12.66 | 1.47 | 1711.00 | -4408.26 | -32199.60 | 27791.30 | -1.17 | -9.24 | 3.91 |
| $H_1L^2$ | 12.65 | 7.74 | 10.93 | 5.29 | 1.37 | 0.45 | 20.73 | 10.52 | 6.00 | 12.65 | 1.40 | 1813.00 | -4408.32 | -30533.30 | 26125.00 | -1.36 | -9.49 | 6.23 |
| $H_1L^3$ | 11.74 | 7.65 | 10.03 | 5.35 | 1.16 | 0.50 | 18.78 | 9.63 | 5.50 | 11.74 | 1.41 | 1417.00 | -3733.38 | -26701.30 | 22967.90 | -0.33 | -9.10 | 3.98 |
| $H_1L^4$ | 11.74 | 7.75 | 10.03 | 5.46 | 1.16 | 0.54 | 18.78 | 9.63 | 5.50 | 11.74 | 1.41 | 1417.00 | -3937.62 | -26768.20 | 22830.60 | -0.44 | -9.38 | 3.75 |
| 1 | 19.44 | 23.38 | 18.25 | 31.56 | 3.99 | 14.21 | 28.75 | 10.57 | 3.90 | 19.44 | 1.27 | 4048.00 | -6525.02 | -62904.40 | 56379.30 | -1.24 | -8.92 | 5.56 |
| 2 | 17.32 | 24.38 | 16.22 | 34.94 | 4.27 | 18.18 | 27.56 | 10.19 | 4.23 | 17.32 | 1.48 | 3254.00 | -6126.06 | -57381.80 | 51255.80 | -1.25 | -8.80 | 5.00 |
| 3 | 14.15 | 22.95 | 14.99 | 36.50 | 5.57 | 26.63 | 21.83 | 7.00 | 3.23 | 14.15 | 1.35 | 2082.00 | -5191.14 | -41526.90 | 36335.80 | -1.24 | -8.89 | 6.38 |
| 4 | 22.08 | 22.94 | 19.99 | 29.16 | 3.48 | 9.78 | 32.22 | 12.40 | 4.26 | 22.08 | 1.26 | 5241.00 | -6986.14 | -73397.70 | 66411.60 | -0.94 | -8.93 | 5.03 |
| 5 | 18.91 | 24.43 | 16.89 | 32.99 | 3.75 | 13.37 | 30.46 | 11.94 | 4.73 | 18.91 | 1.55 | 3921.00 | -6387.54 | -64797.60 | 58410.00 | -0.77 | -8.80 | 5.42 |
| 6 | 14.15 | 22.29 | 14.99 | 34.31 | 5.57 | 23.87 | 21.83 | 7.00 | 3.23 | 14.15 | 1.35 | 2082.00 | -4985.17 | -40827.90 | 35842.80 | -0.84 | -8.86 | 6.76 |
| 7 | 19.42 | 23.38 | 18.32 | 31.59 | 4.05 | 14.23 | 28.75 | 10.57 | 3.97 | 19.42 | 1.23 | 4234.00 | -6525.15 | -60517.00 | 53991.80 | -1.56 | -9.12 | 12.94 |
| 8 | 17.31 | 24.37 | 16.28 | 34.97 | 4.33 | 18.20 | 27.56 | 10.19 | 4.32 | 17.31 | 1.42 | 3416.00 | -6126.21 | -55215.30 | 49089.10 | -1.55 | -9.00 | 12.66 |
| 9 | 14.13 | 22.95 | 15.06 | 36.53 | 5.63 | 26.65 | 21.83 | 7.00 | 3.31 | 14.13 | 1.28 | 2208.00 | -5191.32 | -39731.60 | 34540.30 | -1.57 | -9.05 | 13.04 |
| 10 | 22.06 | 22.93 | 20.06 | 29.19 | 3.54 | 9.81 | 32.22 | 12.40 | 4.32 | 22.06 | 1.22 | 5457.00 | -6986.31 | -71004.80 | 64018.50 | -1.24 | -9.09 | 9.77 |
| 11 | 18.89 | 24.43 | 16.95 | 33.02 | 3.82 | 13.39 | 30.46 | 11.94 | 4.83 | 18.89 | 1.50 | 4101.00 | -6387.75 | -62731.50 | 56343.80 | -1.19 | -8.96 | 10.10 |
| 12 | 14.13 | 22.28 | 15.06 | 34.34 | 5.63 | 23.89 | 21.83 | 7.00 | 3.31 | 14.13 | 1.28 | 2208.00 | -4985.41 | -39475.80 | 34490.40 | -1.21 | -8.97 | 10.03 |
| 13 | 18.51 | 23.29 | 17.42 | 31.65 | 3.84 | 14.29 | 26.87 | 9.79 | 3.62 | 18.51 | 1.26 | 3564.00 | -5850.19 | -55900.80 | 50050.60 | -1.09 | -8.64 | 7.54 |
| 14 | 16.39 | 24.28 | 15.38 | 35.03 | 4.12 | 18.26 | 25.64 | 9.39 | 3.92 | 16.39 | 1.45 | 2830.00 | -5451.20 | -51152.20 | 45701.00 | -1.10 | -8.56 | 7.42 |
| 15 | 13.22 | 22.86 | 14.16 | 36.59 | 5.42 | 26.71 | 19.93 | 6.26 | 2.93 | 13.22 | 1.32 | 1754.00 | -4516.36 | -35696.70 | 31180.30 | -1.11 | -8.57 | 7.51 |
| 16 | 21.15 | 22.84 | 19.16 | 29.26 | 3.33 | 9.86 | 30.34 | 11.60 | 3.98 | 21.15 | 1.24 | 4679.00 | -6311.32 | -66108.70 | 59797.40 | -0.82 | -8.62 | 2.80 |
| 17 | 17.98 | 24.34 | 16.05 | 33.09 | 3.60 | 13.44 | 28.53 | 11.11 | 4.42 | 17.98 | 1.53 | 3449.00 | -5712.75 | -58046.90 | 52334.20 | -0.56 | -8.50 | 2.93 |
| 18 | 13.22 | 22.20 | 14.16 | 34.41 | 5.42 | 23.95 | 19.93 | 6.26 | 2.93 | 13.22 | 1.32 | 1754.00 | -4310.42 | -35432.70 | 31122.20 | -0.40 | -8.51 | 3.03 |
| 19 | 18.51 | 23.38 | 17.42 | 31.76 | 3.84 | 14.32 | 26.87 | 9.79 | 3.62 | 18.51 | 1.26 | 3564.00 | -6054.38 | -54885.10 | 48830.70 | -1.45 | -8.77 | 4.15 |
| 20 | 16.39 | 24.38 | 15.38 | 35.15 | 4.12 | 18.29 | 25.64 | 9.39 | 3.92 | 16.39 | 1.45 | 2830.00 | -5655.43 | -51208.00 | 45552.60 | -1.20 | -8.69 | 8.71 |
| 21 | 13.22 | 22.95 | 14.16 | 36.71 | 5.42 | 26.74 | 19.93 | 6.26 | 2.93 | 13.22 | 1.32 | 1754.00 | -4720.59 | -35778.20 | 31057.60 | -1.22 | -8.71 | 8.80 |
| 22 | 21.15 | 22.94 | 19.16 | 29.37 | 3.33 | 9.89 | 30.34 | 11.60 | 3.98 | 21.15 | 1.24 | 4679.00 | -6515.56 | -66196.20 | 59680.60 | -0.92 | -8.77 | 4.67 |
| 23 | 17.98 | 24.43 | 16.05 | 33.20 | 3.60 | 13.48 | 28.53 | 11.11 | 4.42 | 17.98 | 1.53 | 3449.00 | -5916.95 | -58293.50 | 52376.50 | -0.62 | -8.64 | 4.84 |
| 24 | 13.22 | 22.29 | 14.16 | 34.52 | 5.42 | 23.98 | 19.93 | 6.26 | 2.93 | 13.22 | 1.32 | 1754.00 | -4514.66 | -35513.30 | 30998.60 | -0.50 | -8.64 | 4.93 |

TABLE-5
OBSERVED, PREDICTED AND RESIDUAL ANTIMICROBIAL ACTIVITY OF SCHIFF BASES DERIVED FROM 2-BENZOYL PYRIDINE WITH 2- AND 4-SUBSTITUTED BENZOIC ACID HYDRAZIDES AND THEIR DI/TRIORGANOTIN(IV) COMPLEXES

| Comp. | pMICec MLR | | | pMICpa MLR | | | pMICbc MLR | | | pMICan MLR | | | pMICaf | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Obs | Pre | Res | Obs | Pre | Res | Obs | Pre | Res | Obs | Pre | Res | Obs | Pre | Res |
| $H_1L^1$ | 1.442 | 1.451 | -0.009 | 1.442 | 1.486 | -0.044 | 1.442 | 1.521 | -0.079 | 2.046 | 2.040 | 0.006 | 1.745 | 1.813 | -0.068 |
| $H_1L^2$ | 1.442 | 1.455 | -0.013 | 1.442 | 1.529 | -0.087 | 1.442 | 1.509 | -0.067 | 2.046 | 2.121 | -0.075 | 1.745 | 1.813 | -0.068 |
| $H_1L^3$ | 1.402 | 1.390 | 0.012 | 1.402 | 1.484 | -0.082 | 1.402 | 1.493 | -0.091 | 1.703 | 1.668 | 0.035 | 1.703 | 1.810 | -0.107 |
| $H_1L^4$ | 1.429 | 1.389 | 0.040 | 1.730 | 1.483 | 0.247 | 1.730 | 1.493 | 0.237 | 1.730 | 1.712 | 0.018 | 2.032 | 1.813 | 0.219 |
| 1 | 2.018 | 1.924 | 0.094 | 2.018 | 2.048 | -0.030 | 1.719 | 2.036 | -0.317 | 2.319 | 2.334 | -0.015 | 2.620 | 2.291 | 0.329 |
| 3 | 1.627 | 1.627 | 0.000 | 2.229 | 2.049 | 0.180 | 1.928 | 1.904 | 0.024 | 2.229 | 2.218 | 0.011 | 2.229 | 2.278 | -0.049 |
| 4 | 2.046 | 2.072 | -0.026 | 2.347 | 2.023 | 0.324 | 2.046 | 2.107 | -0.061 | 2.046 | 2.273 | -0.227 | 2.347 | 2.277 | 0.070 |
| 6 | 1.609 | 1.640 | -0.031 | 1.910 | 2.034 | -0.124 | 1.609 | 1.904 | -0.295 | 1.910 | 2.054 | -0.144 | 2.215 | 2.258 | -0.043 |
| 7 | 2.018 | 1.928 | 0.090 | 2.319 | 2.187 | 0.132 | 2.319 | 2.035 | 0.284 | 2.620 | 2.466 | 0.154 | 2.319 | 2.291 | 0.028 |
| 8 | 1.690 | 1.761 | -0.071 | 2.292 | 2.216 | 0.076 | 1.991 | 1.904 | 0.087 | 2.602 | 2.389 | 0.213 | 2.292 | 2.321 | -0.029 |
| 9 | 1.627 | 1.631 | -0.004 | 2.229 | 2.175 | 0.054 | 1.928 | 1.903 | 0.025 | 2.229 | 2.353 | -0.124 | 2.229 | 2.278 | -0.049 |
| 10 | 2.046 | 2.076 | -0.030 | 2.046 | 2.112 | -0.066 | 2.046 | 2.106 | -0.060 | 2.347 | 2.401 | -0.054 | 2.347 | 2.277 | 0.070 |
| 12 | 1.609 | 1.644 | -0.035 | 1.910 | 2.095 | -0.185 | 1.910 | 1.903 | 0.007 | 2.215 | 2.206 | 0.009 | 2.215 | 2.257 | -0.042 |
| 14 | 1.668 | 1.695 | -0.027 | 2.268 | 2.114 | 0.154 | 1.971 | 1.881 | 0.090 | 1.971 | 2.173 | -0.202 | 2.268 | 2.319 | -0.051 |
| 15 | 1.600 | 1.566 | 0.034 | 1.903 | 2.067 | -0.164 | 1.903 | 1.879 | 0.024 | 2.509 | 2.134 | 0.375 | 2.509 | 2.275 | 0.234 |
| 16 | 2.027 | 2.010 | 0.017 | 2.027 | 1.977 | 0.050 | 2.027 | 2.080 | -0.053 | 2.310 | 2.198 | 0.112 | 2.310 | 2.274 | 0.036 |
| 17 | 1.684 | 1.767 | -0.083 | 1.987 | 2.031 | -0.044 | 1.684 | 1.884 | -0.200 | 1.987 | 1.980 | 0.007 | 2.284 | 2.320 | -0.036 |
| 18 | 1.583 | 1.579 | 0.004 | 1.883 | 1.960 | -0.077 | 1.883 | 1.879 | 0.004 | 1.883 | 1.844 | 0.039 | 2.187 | 2.255 | -0.068 |
| 21 | 1.618 | 1.565 | 0.053 | 1.921 | 2.095 | -0.174 | 1.921 | 1.879 | 0.042 | 1.921 | 2.178 | -0.257 | 2.222 | 2.278 | -0.056 |
| 22 | 2.041 | 2.010 | 0.031 | 2.041 | 2.016 | 0.025 | 2.337 | 2.080 | 0.257 | 2.337 | 2.236 | 0.101 | 2.337 | 2.277 | 0.060 |
| 23 | 1.699 | 1.766 | -0.067 | 2.000 | 2.070 | -0.070 | 2.000 | 1.884 | 0.116 | 2.000 | 2.003 | -0.003 | 2.000 | 2.323 | -0.323 |
| 24 | 1.600 | 1.579 | 0.021 | 1.903 | 1.999 | -0.096 | 1.903 | 1.879 | 0.024 | 1.903 | 1.884 | 0.019 | 2.201 | 2.258 | -0.057 |

A graph was drawn between observed and predicted antibacterial activity which showed closeness between these two outcomes as depicted in Fig. 1. Another plot was drawn between observed and residual antibacterial activity of the synthesized complexes against *E. coli* which demonstrated that the error of estimation propagated on both side of zero, thus confirming the fact that there was no systematic error in model generation [20] as shown in Fig. 2.

**QSAR model for antifungal activity against *A. niger***

$$pMIC_{an} = - 0.488\ LUMO + 1.644 \quad (5)$$

$n = 22$, $r = 0.728$, $r^2 = 0.618$, $q^2 = 0.443$, $s = 0.183$, $F = 22.498$

**QSAR model for antifungal activity against *A. niger***

$$pMIC_{anMLR} = 0.036\ ^2\chi - 0.408\ LUMO + 1.174 \quad (6)$$

$n = 22$, $r = 0.831$, $r^2 = 0.691$, $q^2 = 0.614$, $s = 0.152$, $F = 21.238$

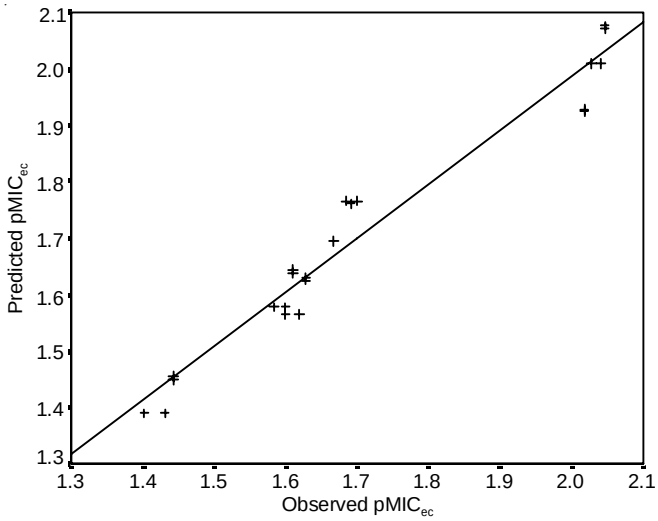


Fig. 1. Plot of observed pMIC$_{ec}$ against the predicted pMIC$_{ec}$ for the linear regression model developed by eqn. 1

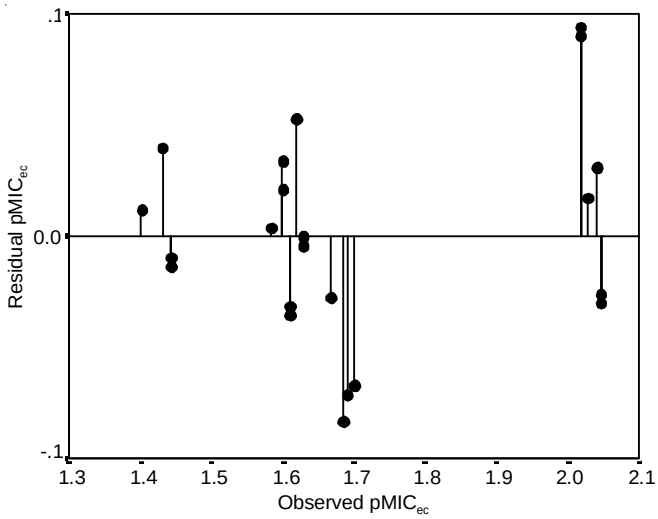


Fig. 2. Plot of residual pMIC$_{ec}$ against the observed pMIC$_{ec}$ for the linear regression model developed by eqn. 2

The correlation analysis study for antifungal activity of synthesized compounds against *A. niger* with various molecular descriptors depicted the prominent role of energy of lowest unoccupied molecular orbital (LUMO) in modifying the antifungal activity (eqn. 5). The linear regression model represented by eqn. 5 was transformed into multiple linear regression model (eqn. 6) which highlighted the additional involvement of second order connectivity index $^2\chi$ along with LUMO for the moderation of antifungal activity [21]. The MLR model represented by eqn. 6 has got high r, $r^2$ and $q^2$ values in comparison to eqn. 5 so this model was used for prediction of antifungal activity of the compounds under current study.

**QSAR model for antifungal activity against *A. flavus***

$$pMIC_{af} = 0.031\ ^1\chi^v + 1.576 \quad (7)$$

n = 22, r = 0.814, $r^2$ = 0.663, $q^2$ = 0.579, s = 0.137, F = 39.250

The monoparametric model (eqn. 7) regarding antifungal activity of synthesized compounds against *A. flavus* demonstrated the importance of valence first order molecular connectivity index $^1\chi^v$ in determining the antifungal activity. The coefficient of $^1\chi^v$ is positive in eqn. 7 which indicated that the antifungal activity will increase with increase in $^1\chi^v$ values.

**QSAR model for antibacterial activity against *B. cereus***

$$pMIC_{bcMLR} = 0.054\ ^2\chi - 0.064\ \kappa_3 + 1.306 \quad (8)$$

n = 22, r = 0.831, $r^2$ = 0.691, $q^2$ = 0.614, s = 0.152, F = 21.238

The QSAR analysis for antibacterial activity of synthesized compounds against *B. cereus* resulted in a biparametric model represented by eqn. 8 which depicted the involvement of second order molecular connectivity index $^2\chi$ and third order kappa shape index ($\kappa_3$) in alteration of antibacterial activity of synthesized compounds. Similar to eqn. 2, QSAR model represented by eqns. 3-8 have got high r, $r^2$ and $q^2$ values and low s values which supported the validity of these derived QSAR models (Table-6). No statistically valid QSAR model was obtained for antibacterial activity of synthesized compounds against *S. aureus*.

TABLE-6
CORRELATION OF MOLECULAR DESCRIPTORS WITH ANTIMICROBIAL ACTIVITY OF SCHIFF BASES DERIVED FROM 2-BENZOYL PYRIDINE WITH 2- AND 4-SUBSTITUTED BENZOIC ACID HYDRAZIDES AND THEIR DI/TRIORGANOTIN(IV) COMPLEXES

| | pMICec | pMICpa | pMICbc | pMICsa | pMICan | pMICaf |
|---|---|---|---|---|---|---|
| $^0\chi$ | 0.943 | 0.666 | 0.656 | 0.523 | 0.542 | 0.603 |
| $^0\chi^v$ | 0.871 | 0.779 | 0.744 | 0.581 | 0.510 | 0.723 |
| $^1\chi$ | 0.949 | 0.609 | 0.636 | 0.500 | 0.514 | 0.564 |
| $^1\chi^v$ | 0.607 | 0.836 | 0.713 | 0.604 | 0.475 | 0.814 |
| $^2\chi$ | 0.958 | 0.762 | 0.753 | 0.627 | 0.593 | 0.753 |
| $^2\chi^v$ | 0.433 | 0.779 | 0.635 | 0.563 | 0.413 | 0.773 |
| $^3\chi$ | 0.157 | 0.582 | 0.438 | 0.422 | 0.287 | 0.625 |
| $^3\chi^v$ | 0.016 | 0.520 | 0.361 | 0.380 | 0.224 | 0.554 |
| $\kappa_1$ | 0.894 | 0.595 | 0.578 | 0.449 | 0.498 | 0.499 |
| $\kappa_2$ | 0.548 | 0.075 | 0.133 | 0.058 | 0.198 | -0.043 |
| $\kappa_3$ | -0.231 | -0.547 | -0.500 | -0.442 | -0.233 | -0.675 |
| R | 0.949 | 0.609 | 0.636 | 0.500 | 0.514 | 0.564 |
| J | -0.625 | -0.350 | -0.533 | -0.547 | -0.457 | -0.538 |
| W | 0.942 | 0.579 | 0.616 | 0.495 | 0.519 | 0.526 |
| Te | -0.936 | -0.712 | -0.663 | -0.559 | -0.612 | -0.619 |
| EleE | -0.933 | -0.665 | -0.638 | -0.495 | -0.516 | -0.599 |
| NuE | 0.932 | 0.661 | 0.635 | 0.490 | 0.509 | 0.597 |
| LUMO | -0.264 | -0.396 | -0.269 | -0.550 | -0.728 | -0.276 |
| HOMO | 0.223 | 0.378 | 0.359 | 0.218 | -0.003 | 0.500 |
| M | 0.144 | 0.481 | 0.383 | 0.622 | 0.599 | 0.274 |

## Conclusion

QSAR studies showed the importance of second order molecular connectivity index in modulating the antibacterial potential of synthesized compounds against *E. coli.* The monoparametric model regarding antifungal activity of synthesized compounds against *A. flavus* demonstrated the importance of valence first order molecular connectivity index $^1\chi^v$ in determining the antifungal activity. QSAR analysis for *P. aeruginosa* depicted the involvement of valence first order molecular connectivity index ($^1\chi^v$) was the determinant molecular descriptor responsible for antibacterial activity. QSAR analysis for *B. cereus* resulted in a biparametric model which depicted the involvement of second order molecular connectivity index $^2\chi$ and third order kappa shape index ($\kappa_3$) in alteration of antibacterial activity of synthesized compounds. The correlation

analysis study for antifungal activity of synthesized compounds against *A. niger* with various molecular descriptors depicted the prominent role of energy of lowest unoccupied molecular orbital (LUMO) in modifying the antifungal activity. No statistically valid QSAR model was obtained for antibacterial activity of synthesized compounds against *S. aureus*.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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