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Correlation of antibacterial activity of some *N*-[5-(2-furanyl)-2-methyl-4-oxo-4*H*-thieno[2,3-*d*]pyrimidin-3-yl]-carboxamide and 3-substituted-5-(2-furanyl)-2-methyl-3*H*-thieno[2,3-*d*]pyrimidin-4-ones with topological indices using Hansch analysis

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Abstract—The antimicrobial activity of the *N*-[5-(2-furanyl)-2-methyl-4-oxo-4*H*-theino[2,3-*d*]pyrimidin-3-y1]-carboxamides and 3-substituted-5-(2-furanyl)-2-methyl-3*H*-thieno[2,3-*d*]pyrimidin4-ones was correlated with different topological indices using Hansch analysis. Good correlations were obtained through a simple regression equation with third order molecular connectivity index ($^3\chi$). The developed QSAR models were crossvalidated by leave-one-out technique.

The importance of substituted thienopyrimidines and thienopyrimidenes is well established. Literature reports reveal their anti-inflammatory,[1,2] antimalarial,[3] and antibacterial[4–6] activities. Quantitative structure–activity relationship (QSAR) has been traditionally perceived as a means of establishing correlation between trends in chemical structure modifications and respective changes of biological activity.[7]

As part of our efforts to create QSAR models that show substantial predictive promise for the design of new compounds with improved biological activity, we have previously reported the QSAR studies for antimicrobial activity[8–11] and anti-inflammatory activity.[12] From the results of our earlier studies we have noted that the distance based topological indices are effective in describing antimicrobial activity and are widely used in QSAR studies.

In the present work, we correlated the antibacterial activity of substituted thienopyrimidones and thienopyrimidyl carboxamides with topological indices.[13–23] Structures of thienopyrimidyl carboxamide and thienopyrimidones and their antibacterial potential in terms of −log MIC values against Gram-positive *Staphylococcus aureus*, *Bacillus subtilis* and Gram-negative *Escherichia coli* and *Salmonella typhi* as well as against *Mycobacterium tuberculosis* and *Mycobacterium avium* reported by Chambhare et al.,[6] are presented in Table 1.

In attempting QSAR, the antimicrobial data given in terms of minimum inhibitory concentration (MIC in μM) were converted into log[1/MIC], that is, −log MIC and used as a dependent variable. The topological indices (independent variables) molecular connectivity indices [$\chi, {}^1\chi, {}^2\chi, {}^3\chi$], valence order molecular connectivity indices [$^0\chi^v, {}^1\chi^v, {}^2\chi^v, {}^3\chi^v$], Kiers shape indices [$\kappa_1, \kappa_2, \kappa_3, \kappa\alpha_1, \kappa\alpha_2, \kappa\alpha_3$], Randic [*R*], Balban [*J*], and Wiener [*W*] topological indices were calculated by the molecular package TSAR 3D version for Windows[24] and the values are presented in Table 2. The perusal of Table 3 of correlation matrix demonstrated that out of the 15 topological indices used the zero, second, and third order molecular connectivity indices,

Keywords: Thienopyrimidones; Antibacterial activity; QSAR; Topological indices; q^2.
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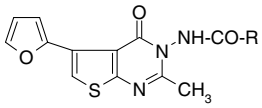
Table 1. Chemical structure and antibacterial activity of *N*-[5-(2-furanyl)-2-methyl-4-oxo-4*H*-thieno[2,3-*d*]pyrimidin-3-yl]-carboxamide and 3-substituted-5-(2-furanyl)-2-methyl-3*H*-thieno[2,3-*d*]pyrimidin-4-ones[6]



1-13

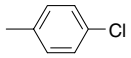
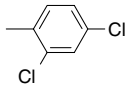
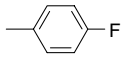
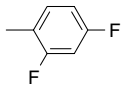
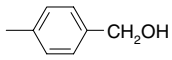
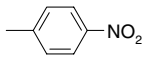
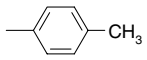
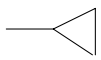
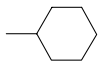
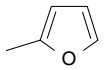
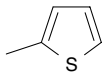
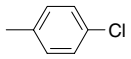
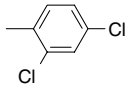
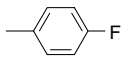
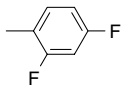
Compound	R	$-\log MIC_{SA}$	$-\log MIC_{BS}$	$-\log MIC_{EC}$	$-\log MIC_{ST}$	$-\log MIC_{MT}$	$-\log MIC_{MA}$
1		1.30	1.26	1.27	1.38	1.30	1.32
2		2.00	2.05	2.00	1.92	2.05	2.10
3		2.30	2.40	2.22	2.22	2.30	2.40
4		2.05	2.05	2.05	1.96	2.05	2.05
5		2.40	2.30	2.40	2.30	2.40	2.40
6		2.00	2.05	2.00	1.92	2.05	2.10
7		2.22	2.30	2.15	2.22	2.22	2.22
8		1.52	1.34	1.26	1.32	1.39	1.40
9	CH_3	1.26	1.19	1.15	1.01	1.11	1.07
10		1.25	1.24	1.22	0.97	1.06	1.05
11		1.23	1.22	1.18	1.01	0.98	1.06
12		1.30	1.25	1.19	1.11	1.39	1.40
13		1.29	1.26	1.22	1.13	1.34	1.35
14		1.26	1.23	1.19	1.18	1.30	1.32
15		2.00	2.05	2.05	2.10	2.05	2.00
16		2.40	2.40	2.22	2.30	2.40	2.40
17		2.00	2.05	2.05	2.10	2.05	2.00
18		2.30	2.40	2.30	2.22	2.40	2.40

Table 1 (*continued*)

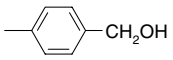
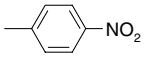
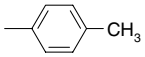
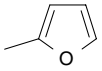
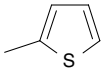
Compound	R	$-\log MIC_{SA}$	$-\log MIC_{BS}$	$-\log MIC_{EC}$	$-\log MIC_{ST}$	$-\log MIC_{MT}$	$-\log MIC_{MA}$
19		1.96	1.96	1.92	1.92	1.85	1.85
20		2.40	2.30	2.15	2.15	2.22	2.22
21		1.24	1.25	1.23	1.19	1.28	1.25
22	CH_3	1.19	1.16	1.13	1.12	1.22	1.24
23		1.19	1.18	1.15	1.15	1.18	1.23
24		1.19	1.14	1.11	1.12	1.19	1.24
25		1.24	1.23	1.21	1.19	1.28	1.21
26		1.24	1.25	1.16	1.19	1.30	1.28

Table 2. Calculated topological indices for thieno compounds used in the present study

Compound	$^0\chi$	$^0\chi^v$	$^1\chi$	$^2\chi$	$^3\chi$	$^3\chi^v$	κ_1	κ_2	κ_3	$\kappa\alpha_1$	$\kappa\alpha_2$	$\kappa\alpha_3$	R	W	Te
1	17.39	14.11	12.15	10.97	1.55	0.67	18.37	7.94	3.70	16.30	6.61	2.96	12.15	1470.00	−4255.77
2	18.26	15.22	12.54	11.59	1.84	0.87	19.32	8.16	3.94	17.52	7.02	3.28	12.54	1664.00	−4615.84
3	19.13	16.34	12.95	12.13	2.04	1.03	20.28	8.39	4.02	18.75	7.43	3.47	12.95	1824.00	−4975.79
4	18.26	14.41	12.54	11.59	1.84	0.74	19.32	8.16	3.94	17.18	6.81	3.16	12.54	1664.00	−4727.15
5	19.13	14.71	12.95	12.13	2.04	0.78	20.28	8.39	4.02	18.06	7.01	3.23	12.95	1824.00	−5198.39
6	18.97	15.44	13.08	11.76	1.75	0.74	20.28	8.79	4.16	18.16	7.42	3.38	13.08	1884.00	−4731.64
7	19.84	15.29	13.45	12.49	2.05	0.79	21.24	9.01	4.40	18.73	7.42	3.47	13.45	2106.00	−5086.60
8	18.26	15.03	12.54	11.59	1.84	0.84	19.32	8.16	3.94	17.24	6.85	3.18	12.54	1664.00	−4411.63
9	14.28	11.72	9.58	8.99	1.55	0.64	14.92	6.01	2.85	13.58	5.18	2.37	9.58	757.00	−3588.83
10	15.27	12.71	10.65	9.91	1.55	0.74	15.52	6.14	2.71	14.21	5.35	2.29	10.65	1004.00	−3871.29
11	17.39	14.83	12.15	10.97	1.55	0.74	18.37	7.94	3.70	17.04	7.08	3.22	12.15	1470.00	−4340.27
12	16.68	13.62	11.65	10.62	1.55	0.65	17.42	7.32	3.36	15.81	6.31	2.80	11.65	1298.00	−4319.90
13	16.68	14.50	11.65	10.62	1.55	0.78	17.42	7.32	3.36	16.17	6.54	2.92	11.65	1298.00	−4194.38
14	15.81	13.15	11.24	10.10	1.35	0.61	16.47	7.09	3.25	14.95	6.12	2.72	11.24	1148.00	−3792.30
15	16.68	14.26	11.63	10.72	1.64	0.81	17.42	7.32	3.49	16.16	6.53	3.03	11.63	1314.00	−4152.42
16	17.55	15.38	12.04	11.25	1.84	0.97	18.37	7.55	3.58	17.39	6.94	3.22	12.04	1450.00	−4512.47
17	16.68	13.45	11.63	10.72	1.64	0.67	17.42	7.32	3.49	15.82	6.32	2.91	11.63	1314.00	−4263.74
18	17.55	13.75	12.04	11.25	1.84	0.72	18.37	7.55	3.58	16.70	6.52	2.99	12.04	1450.00	−4735.10
19	17.39	14.48	12.17	10.89	1.55	0.68	18.37	7.94	3.70	16.80	6.93	3.13	12.17	1504.00	−4268.22
20	18.26	14.33	12.54	11.62	1.85	0.72	19.32	8.16	3.94	17.37	6.93	3.22	12.54	1696.00	−4623.21
21	16.68	14.07	11.63	10.72	1.64	0.77	17.42	7.32	3.49	15.89	6.36	2.94	11.63	1314.00	−3948.19
22	13.41	11.34	9.22	8.15	1.14	0.53	13.96	5.78	2.49	13.04	5.20	2.18	9.22	654.00	−3268.15
23	14.40	12.33	10.24	9.38	1.35	0.70	14.58	5.89	2.59	13.69	5.35	2.30	10.24	895.00	−3550.63
24	16.52	14.45	11.74	10.44	1.35	0.70	17.42	7.71	3.62	16.51	7.11	3.28	11.74	1348.00	−4019.60
25	15.81	12.98	11.24	10.09	1.35	0.60	16.47	7.09	3.25	15.03	6.17	2.74	11.24	1181.00	−3970.73
26	15.81	13.86	11.24	10.09	1.35	0.75	16.47	7.09	3.25	15.40	6.40	2.87	11.24	1181.00	−3845.67

$[^0\chi, ^2\chi, ^3\chi]$, and Kiers shape indices $[\kappa_1, \kappa\alpha_1]$ are best for modeling against all the organisms.

The data presented in Table 4 show that the topological parameters are significantly correlated with the antibacterial activity against *S. aureus*. The mono-parametric model based on $^3\chi$ (Eq. 1) was found to be best for explaining antibacterial activity of title compounds. The $^3\chi$ being a topological parameter of molecular connectivity has the ability to emphasize different aspects of atom connectivity within a molecule viz. the amount of branching and flexibility of the molecules.

Table 3. Correlation matrix of antibacterial activity of thieno compounds against *Staphylococcus aureus*

	$-\log MIC_{SA}$	$^0\chi$	$^0\chi^v$	$^1\chi$	$^2\chi$	$^3\chi$	$^3\chi^v$	κ_1	κ_2	κ_3	$\kappa\alpha_1$	$\kappa\alpha_2$	$\kappa\alpha_3$	*R*	*B*	*W*	Te
$-\log MIC_{SA}$	1.000																
$^0\chi$	0.733	1.000															
$^0\chi^v$	0.594	0.904	1.000														
$^1\chi$	0.669	0.986	0.916	1.000													
$^2\chi$	0.736	0.991	0.901	0.984	1.000												
$^3\chi$	0.832	0.870	0.725	0.793	0.885	1.000											
$^3\chi^v$	0.549	0.614	0.789	0.579	0.652	0.710	1.000										
κ_1	0.725	0.998	0.899	0.981	0.981	0.857	0.589	1.000									
κ_2	0.631	0.970	0.894	0.977	0.942	0.739	0.494	0.979	1.000								
κ_3	0.669	0.973	0.885	0.969	0.951	0.787	0.523	0.982	0.992	1.000							
$\kappa\alpha_1$	0.729	0.982	0.952	0.973	0.969	0.830	0.673	0.983	0.966	0.966	1.000						
$\kappa\alpha_2$	0.602	0.918	0.949	0.942	0.896	0.659	0.585	0.926	0.960	0.945	0.964	1.000					
$\kappa\alpha_3$	0.644	0.926	0.947	0.938	0.910	0.714	0.623	0.934	0.956	0.959	0.970	0.990	1.000				
R	0.669	0.986	0.916	1.000	0.984	0.793	0.579	0.981	0.977	0.969	0.973	0.942	0.938	1.000			
B	−0.341	−0.664	−0.695	−0.769	−0.713	−0.375	−0.380	−0.637	−0.688	−0.660	−0.660	−0.719	−0.695	−0.769	1.000		
W	0.706	0.993	0.893	0.987	0.979	0.831	0.573	0.993	0.978	0.976	0.975	0.925	0.927	0.987	−0.689	1.000	
Te	−0.812	−0.961	−0.818	−0.926	−0.959	−0.912	−0.594	−0.953	−0.890	−0.898	−0.937	−0.833	−0.845	−0.926	0.560	−0.939	1.000

QSAR model for antibacterial activity against *S. aureus*

$$-\log MIC_{SA} = 1.644\,^3\chi - 1.011$$
$$n = 26,\ r = 0.832,\ q^2 = 0.647,$$
$$F = 53.93,\ s = 0.27 \quad (1)$$

The positive coefficient of $^3\chi$ in mono-parametric model represented by Eq. 1 indicates that the antibacterial activity of thieno compounds against *S. aureus* is directly proportional to the magnitude of $^3\chi$, that is, the increase in the magnitude of $^3\chi$ increases the antibacterial activity. The compounds **3**, **5**, and **7** having the maximum $^3\chi$ values of 2.04, 2.04 and 2.05 (Table 2), respectively, are found to be most effective ones than any other compounds included in the present study. Similarly, the least active compound is **22** because of its low $^3\chi$ value ($^3\chi$ = 1.14, $-\log MIC_{SA}$ = 1.13).

Further it is important to note that the substituted electron-poor aromatic residues (compounds **2**–**7** and **15**–**20**, Table 1) are the most active ones having high $^3\chi$ values in the range of 1.84–2.04 and 1.64–1.85 (Table 2) in case of thienopyrimidyl carboxamides (**1**–**13**) and thienopyrimidones (**14**–**26**), respectively. While, the alkyl- and non-substituted, electron-rich aromatic residues (compounds **9**–**14** and **22**–**26**, Table 1) are less active due to their low $^3\chi$ values in the range of 1.55 and 1.14–1.35 (Table 2).

The only exception is the *para*-benzylalcohol residue (compounds **6** and **19**, Table 1), an alkyl-substituted compound having better activity. In this case, the hydroxy group present might interact specifically with the target which may be responsible for its better activity even though it contains alkyl substitution on aromatic ring. This is evidenced by its $^3\chi$ value of 1.75 and 1.55 which is closer to the range of 1.84 and 1.64 in case of thienopyrimidyl carboxamides and thienopyrimidones, respectively. The other exception is the toluene residue (compounds **8** and **21**), which showed a marginal increase in the antibacterial activity even though it had a better $^3\chi$ value of 1.84 and 1.64 which is equal to the range of most active compounds. This may be due to the fact that the electron-rich nature of toluene residue may be responsible for its poor interaction with the target.

The QSAR model expressed by Eq. 1 was crossvalidated by its crossvalidated correlation coefficient value (q^2 = 0.600) obtained by 'leave one out' method, where a model is built with $N-1$ compounds and the Nth compound is predicted. Each compound is left out of the model derivation and predicted in turn. The value of q^2 is the basic requirement for declaring a model to be a valid one is $q^2 > 0.5$.[25] The predictive ability of the QSAR model (Eq. 1) has been proved by the plot of observed $-\log MIC_{SA}$ and calculated $-\log MIC_{SA}$ (Fig. 1).

When bacterial inhibition data (Table 1) were correlated with electrotopological parameters, the statistical parameters showed the following significant QSAR models from Eqs. 2–6.

Table 4. Correlation of different parameters with biological activity

Molecular descriptor	$-\log MIC_{SA}$	$-\log MIC_{BS}$	$-\log MIC_{EC}$	$-\log MIC_{ST}$	$-\log MIC_{MT}$	$-\log MIC_{MA}$
$^0\chi$	0.733	0.720	0.713	0.712	0.712	0.732
$^0\chi^v$	0.594	0.593	0.568	0.582	0.580	0.611
$^1\chi$	0.669	0.660	0.654	0.661	0.656	0.676
$^2\chi$	0.736	0.725	0.718	0.716	0.716	0.733
$^3\chi$	0.832	0.814	0.805	0.778	0.793	0.801
$^3\chi^v$	0.549	0.555	0.514	0.516	0.527	0.552
κ_1	0.725	0.711	0.704	0.705	0.703	0.724
κ_2	0.631	0.619	0.613	0.627	0.617	0.638
κ_3	0.669	0.655	0.649	0.664	0.652	0.669
$\alpha\kappa_1$	0.729	0.720	0.705	0.710	0.709	0.734
$\alpha\kappa_2$	0.602	0.599	0.582	0.603	0.593	0.621
$\alpha\kappa_3$	0.644	0.639	0.622	0.643	0.632	0.655
R	0.669	0.660	0.654	0.661	0.656	0.676
B	−0.341	−0.348	−0.347	−0.381	−0.354	−0.362
W	0.706	0.695	0.688	0.693	0.687	0.708
Te	−0.812	−0.801	−0.802	−0.778	−0.796	−0.812

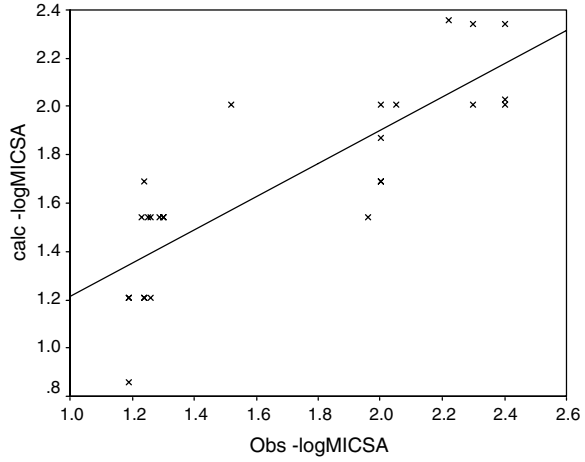


Figure 1. Plot of predicted $-\log MIC$ activity values against the experimental $-\log MIC$ values for the QSAR model by Eq. 1 for *Staphylococcus aureus*.

QSAR model for antibacterial activity against *B. subtilis*

$$-\log MIC_{BS} = 1.692\,{}^3\chi - 1.098$$
$$n = 26,\ r = 0.814,\ q^2 = 0.616,$$
$$F = 47.24,\ s = 0.30 \quad (2)$$

QSAR model for antibacterial activity against *E. coli*

$$-\log MIC_{EC} = 1.611\,{}^3\chi - 1.018$$
$$n = 26,\ r = 0.805,\ q^2 = 0.600,$$
$$F = 44.28,\ s = 0.29 \quad (3)$$

QSAR model for antibacterial activity against *S. typhi*

$$-\log MIC_{ST} = 1.621\,{}^3\chi - 1.064$$
$$n = 26,\ r = 0.777,\ q^2 = 0.554,$$
$$F = 36.75,\ s = 0.37 \quad (4)$$

QSAR model for antibacterial activity against *M. tuberculosis*

$$-\log MIC_{MT} = 1.622\,{}^3\chi - 0.990$$
$$n = 26,\ r = 0.792,\ q^2 = 0.575,$$
$$F = 40.54,\ s = 0.31 \quad (5)$$

QSAR model for antibacterial activity against *M. avium*

$$-\log MIC_{MA} = 1.645\,{}^3\chi - 1.019$$
$$n = 26,\ r = 0.801,\ q^2 = 0.588,$$
$$F = 42.86,\ s = 0.30 \quad (6)$$

As in case of *S. aureus*, the positive value of the correlation coefficient of $^3\chi$ in mono-parametric models demonstrated that the antibacterial activity of thieno compounds is directly proportional to the magnitude of $^3\chi$. The plot of linear regression predicted $-\log MIC$ values against the observed $-\log MIC$ values (Figs. 2–6) favors the QSAR models expressed by Eqs. 2–6. The high q^2 value obtained also supports the models expressed by Eqs. 2–6. The other statistically significant models developed are presented in Table 5. It is noteworthy that all these equations were derived using the entire data set of compounds ($n = 26$) since no outliers were identified.

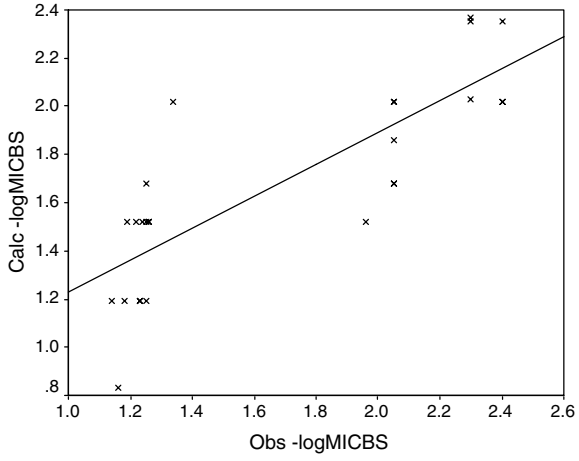


Figure 2. Plot of predicted $-\log MIC$ activity values against the experimental $-\log MIC$ values for the QSAR model by Eq. 2 for *Bacillus subtilis*.

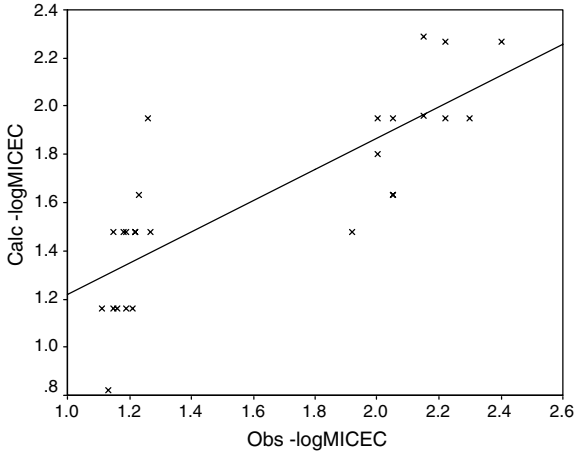


Figure 3. Plot of predicted −log MIC activity values against the experimental −log MIC values for the QSAR model by Eq. 3 for *Escherichia coli*.

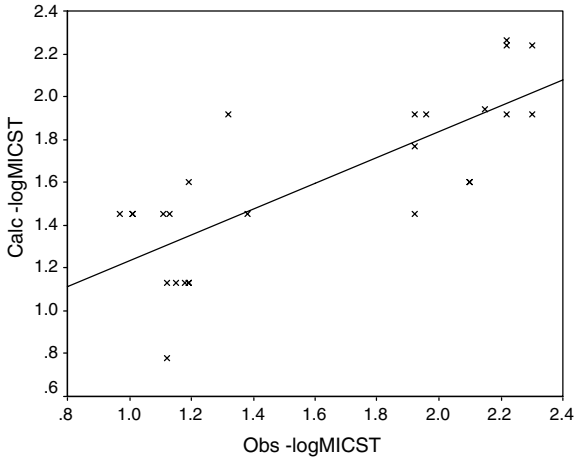


Figure 4. Plot of predicted −log MIC activity values against the experimental −log MIC values for the QSAR model by Eq. 4 for *Salmonella typhi*.

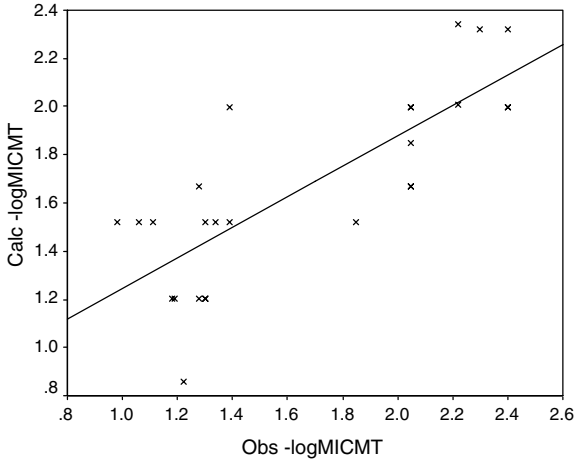


Figure 5. Plot of predicted −log MIC activity values against the experimental −log MIC values for the QSAR model by Eq. 5 for *Mycobacterium tuberculosis*.

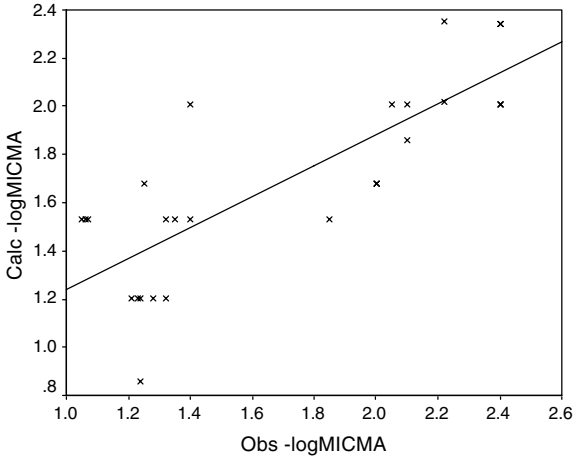


Figure 6. Plot of predicted −log MIC activity values against the experimental −log MIC values for the QSAR model by Eq. 6 for *Mycobacterium avium*.

Even the 'rule of thumb' allowed us to go for a multi-parametric models the high inter-relationship among the molecular descriptors made us to stick to a mono-parametric model. The 'rule of thumb' gives information about the number of parameters to be selected for regression analysis in QSAR based on the number of compounds. According to this rule for a QSAR model development one should select one parameter for a five compound data set. As the number of compounds in the present study (26) allowed us to go up to a maximum of penta-parametric models, the high inter-relationship (auto-correlation) between the parameters restricted us to a single-parametric model. Because, the auto-correlation of molecular descriptors prevents the significant improvement in the statistical parameters of the QSAR models in multiple linear regression (MLR) analysis.

The multicolinearity (auto-correlation) between the parameters[26] is indicated by the change in signs of the coefficients, a change in the values of previous coefficient, change of significant variable into insignificant one or an increase in standard error of the estimate on addition of an additional parameter to the model.

In conclusion, the QSAR study throws some light for the first time on correlation of antibacterial activity of *N*-[5-(2-furanyl)-2-methyl-4-oxo-4*H*-thieno[2,3-*d*]pyrimidin-3-yl]-carboxamide and 3-substituted-5-(2-furanyl)-2-methyl-3*H*-thienopyrimidin-4-ones[2–26] with physicochemical parameters. The QSAR study indicated the importance of topological parameters especially third order molecular connectivity index in describing the antibacterial activity of thieno compounds. Further, the importance of topological parameters in describing in antibacterial activity is similar to the results observed in our earlier studies.[8–11] The QSAR models developed in this work show substantial promise in the prediction of the antibacterial activity of novel thieno analogs, as we search for more potent compounds.

Table 5. Best QSAR models for antibacterial activity of thieno compounds

S. no.	QSAR Models	*n*	*r*	q^2	$F(p < 0.01)$	*S*
	S. aureus					
1	$-\log MIC_S = 0.220^0\chi - 2.069$	26	0.732	0.476	27.86	0.33
2	$-\log MIC_S = 0.350^2\chi - 2.119$	26	0.736	0.456	28.42	0.33
3	$-\log MIC_S = 1.644^3\chi - 1.011$	26	0.831	0.647	53.93	0.27
4	$-\log MIC_S = 0.187\kappa_1 - 1.665$	26	0.725	0.469	26.57	0.34
5	$-\log MIC_S = 0.227\kappa\alpha_1 - 2.020$	26	0.728	0.473	27.15	0.33
	B. subtilis					
6	$-\log MIC_B = 0.227^0\chi - 2.201$	26	0.720	0.458	25.85	0.36
7	$-\log MIC_B = 0.364^2\chi - 2.260$	26	0.724	0.440	26.54	0.35
8	$-\log MIC_B = 1.692^3\chi - 1.098$	26	0.814	0.616	47.24	0.30
9	$-\log MIC_B = 0.193\kappa_1 - 1.780$	26	0.711	0.449	24.55	0.36
10	$-\log MIC_B = 0.236\kappa\alpha_1 - 2.175$	26	0.720	0.462	25.89	0.36
	E. coli					
11	$-\log MIC_E = 0.217^0\chi - 2.074$	26	0.713	0.446	24.88	0.35
12	$-\log MIC_E = 0.347^2\chi - 2.136$	26	0.717	0.429	25.52	0.35
13	$-\log MIC_E = 1.611^3\chi - 1.018$	26	0.805	0.600	44.28	0.29
14	$-\log MIC_E = 0.184\kappa_1 - 1.671$	26	0.704	0.436	23.62	0.35
15	$-\log MIC_E = 0.223\kappa\alpha_1 - 2.007$	26	0.705	0.439	23.75	0.35
	S. typhi					
16	$-\log MIC_{ST} = 0.226^0\chi - 2.251$	26	0.712	0.444	24.70	0.36
17	$-\log MIC_{ST} = 0.360^2\chi - 2.305$	26	0.715	0.423	25.19	0.36
18	$-\log MIC_{ST} = 1.621^3\chi - 1.064$	26	0.777	0.554	36.75	0.32
19	$-\log MIC_{ST} = 0.192\kappa_1 - 1.843$	26	0.705	0.437	23.75	0.37
20	$-\log MIC_{ST} = 0.233\kappa\alpha_1 - 2.211$	26	0.709	0.444	24.34	0.36
	M. tuberculosis					
21	$-\log MIC_{MT} = 0.221^0\chi - 2.106$	26	0.711	0.442	24.64	0.36
22	$-\log MIC_{MT} = 0.354^2\chi - 2.164$	26	0.716	0.420	25.28	0.35
23	$-\log MIC_{MT} = 1.622^3\chi - 0.990$	26	0.792	0.575	40.54	0.31
24	$-\log MIC_{MT} = 0.188\kappa_1 - 1.698$	26	0.703	0.434	23.51	0.36
25	$-\log MIC_{MT} = 0.229\kappa\alpha_1 - 2.065$	26	0.709	0.442	24.26	0.36
	M. avium					
26	$-\log MIC_{MA} = 0.229^0\chi - 2.217$	26	0.731	0.469	27.65	0.35
27	$-\log MIC_{MA} = 0.364^2\chi - 2.259$	26	0.733	0.439	27.88	0.35
28	$-\log MIC_{MA} = 1.645^3\chi - 1.019$	26	0.801	0.588	42.86	0.30
29	$-\log MIC_{MA} = 0.195\kappa_1 - 1.800$	26	0.724	0.462	26.41	0.35
30	$-\log MIC_{MA} = 0.238\kappa\alpha_1 - 2.204$	26	0.734	0.479	28.09	0.35

Antibacterial activity. The antibacterial activity of some *N*-[5-(2-furanyl)-2-methyl-4-oxo-4*H*-thieno[2,3-*d*]pyrimidin-3-yl]-carboxamide and 3-substituted-5-(2-furanyl)-2-methyl-3*H*-thieno[2,3-*d*]pyrimidin-4-ones reported earlier[6] was used after converting it into negative log units.

Topological indices and regression analyses. The details of the calculation of topological indices used in the present study are available in the literature[13–23] and therefore they are not discussed in detail over here. All the topological indices were calculated by using the molecular package TSAR 3D version for Windows. The regression analyses were also performed by the same package.

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