Available online at: http://www.basra-science-journal.ogr

ISSN –1817 –2695

Received 8-9-2016, Accepted 23-4-2017

QSAR STUDIES OF AMINO ACIDS CONJUGATED 2-AMINO-ARYLTHIAZOLE AS ANTI-BACTERIAL

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ABSTRACT

Quantitative structure-activity relationships (QSAR) of 16 thiazole derivatives against five types of bacteria, namely: Klebsiella pneumoniae, Staphylococcus aereus, Escherichia coli, Bacillus substilis and Pseudomonas areginosa, was carried out. Physio-chemical parameters were obtained computationally by optimization of chemical structures at minimum energy using molecular mechanics (MM+) theory and the semi-empirical molecular orbital (AM1) method. Then, multiple linear regression (MLR) analysis used to correlate changes in chemical structure and experimental antibacterial activity. Moreover, it is found that some descriptors are in strong dependences to provide good information and play important roles to evaluate antibacterial activity of thiazole derivatives. Results, 20 equations were found statistically with correlation coefficient rang (0.806-0.955). In addition, within the current QSAR study, the quality of the discriminant models was determined on the basis of correlation coefficient (R^2), Fisher ratio (F), and standard error (S). Consequently, five good models with high correlation coefficient (R^2>0.9) were nominated as valuable theoretical base to improve 15 other subset predicted structures of amino acids conjugated 2-amnio-arylthiazole demonstrating anti-bacterial activity, and most of them showed good antibacterial activities against positive gram of bacteria.

Keywords: *Thiazole, Amino acids, Anti-bacterial, (QSAR) Model*

1. INTRODUCTION

Quantitative structure property/activity relationships (QSPR/QSAR) is a good analysis technique used to correlate chemical structure and specific chemical properties, such melting point, boiling point, glass transition temperature TG and biological activates, by modeling between calculated descriptors obtained from molecular structures and desired property which is got

experimentally, and the results are derived models that help to predict properties/activities of untested chemicals [1]. When little or no more actual databases are available, QSPR/QSAR is scientifically great tool for expecting what property/activity is for uncharted chemicals. These studies provide good interpretations and have successfully assisted chemists to reduce their working time, mistakes, and errors in designing of compounds with desired activity/property [2]. QSPR/QSAR studies generally involve two steps: first, descriptors (physical-chemical parameters) are generated which encode for chemical structural information; and second, a statistical regression method correlates changes in structure with changes in chemical properties or biological activity. The compound in the training set (i.e., the data set selected to construct the QSPR/QSAR model) should be diverse in both chemical structure and property/activity to ensure a statistically robust model. The method typically assumes that chemicals function by a common mechanism. The model is then validated by predicting the property/activity for test set (i.e., a group of chemicals not included among the training-set compounds). One validated, these QSPR/QSAR models can be used to predict desired property/activity of untested chemicals [3].

In the last decades, QSAR models have been applied extensively in various areas and have taken great attention in medical chemistry such as toxicity prediction of single-celled in natural water [4], designing chemicals as narcotics and predict their toxicity [5], subjecting natural isolated polyol esters on QSAR to find optimal narcotic activities and insecticidal activities [6], and improving anti-cancer activates for 12 anti-cancer Schiff-base ligands [7]. Also, many researchers reported of SQAR studies on several steroids types. For example, Correlation of lipophilicity degree of amino-steroids derivatives with descriptors, partition coefficient (LogP) and π, was studied [8,9] In addition, studying the effect of steroid–based drug structures on penetrating the bilayer membrane, and correlate with Passive Diffusion, P–Glycoprotein Active Efflux and P–Glycoprotein inhibitor by using QSAR method [10]. P. Bhattacharya and et al, subjected 30 thiazole and thiadizole derivatives to build potent and selective human adenosine A3 receptor antagonists using QSAR [11, 12]. Potent tri-substituted thiazole derivative was designed by other [13], for cancer therapy as serine-threonine protein kinase inhibitor. QSAR analysis of 19 thiazole derivatives with H_1-antihistamine activity was also carried out, and then elaborated new thiazole derivatives [14]. Tube dilution method used to evaluate experimentally 12 molecules of 2,4-disubstituted thiazole as antimicrobial agents and QSAR analysis showed excellent binding for new thiazole derivative [15]. Antiplatelet activities of 20 thiazole derivatives were correlated successfully using QSAR models [16].

It is thus a primary object of the present research to build QSAR models of 16 molecules set of thiazole derivatives, which are amino acids conjugated 2-amnio-arylthiazole, and study the relationship of obtained descriptors such as hydrogen bonding, energy gap, dipole moment, and etc. with *in-vitro* antibacterial activities against three types of negative bacteria: Klebsiella pneumoniae, Staphylococcus aereus, Escherichia coli, and two types of positive bacteria: Bacillus substilis and Pseudomonas areginosa. Finally, results used to predict antibacterial activities of 15 unprepared molecules of thiazole-amino

acids derivatives.

2. METHOD GEOMETAY OPTIMIZATION

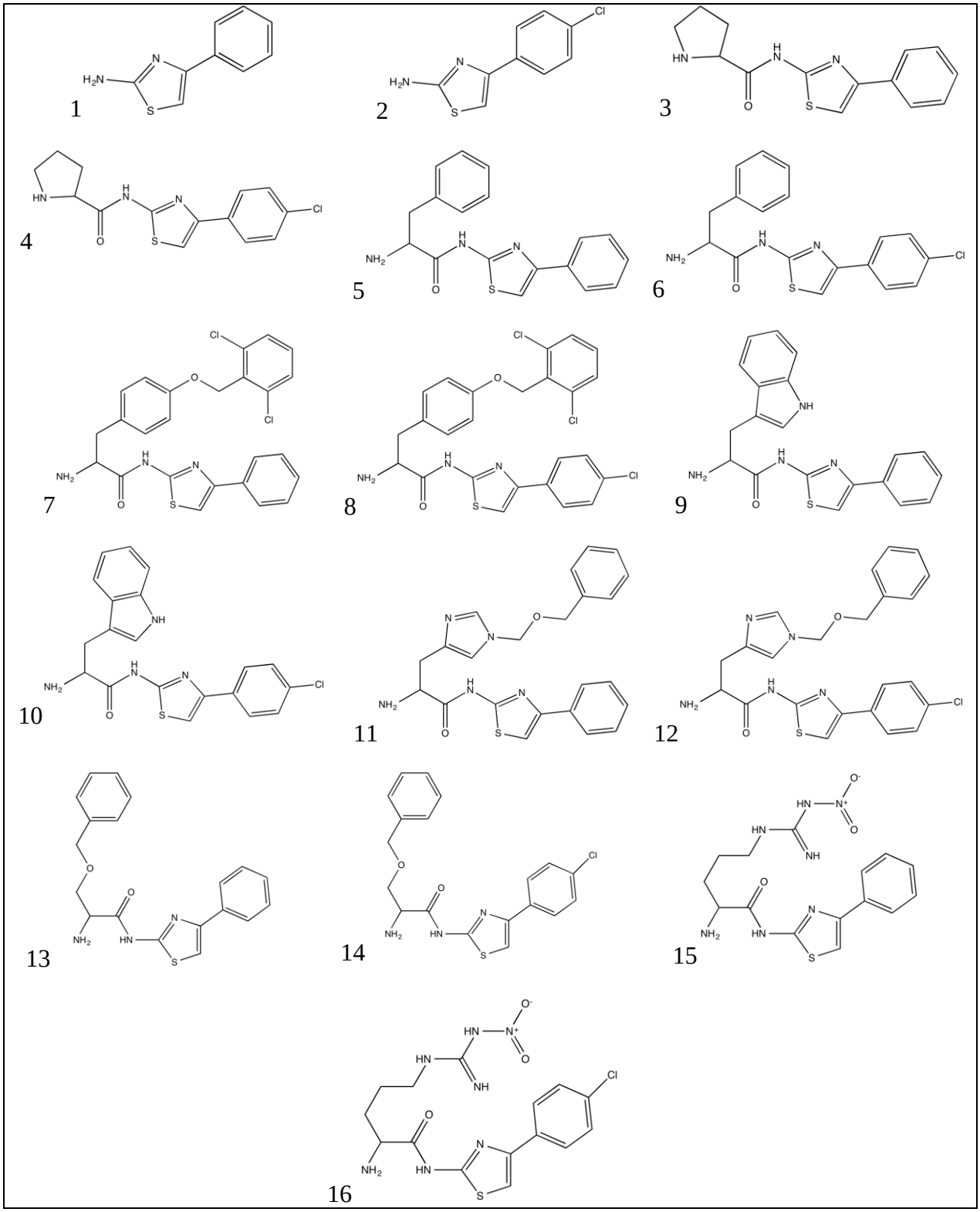
Theoretical calculations were performed by PCGamess, running on a Pentium V PC-CPU 3.4GHz. The geometries of the compounds were optimized first at level (MM+) by molecular mechanics force field theory and then by (AM1) semi-empirical method [17-18]. Then, antibacterial activities of conjugated thiazole-amino acids were regressively utilized for modeling by using multiple liner regression (MLR).

3. EXPERIMANTAL

Antibacterial activities of 16 thiazole molecules against five type of bacteria have been determined experimentally by agar well diffusion method, which a circular well of diameter 6 mm was made exactly at the center of the plates by using cork borer and each well was filled with 0.1 mL of the thiazole-test solution (10mg/mL)[19, 20]. Streptomycin was tested at all agars as standard for thiazole antibacterial. The structures of thiazole derivatives are shown in Figure1, and their experimental inhibitory zones (mm) were also tabled in Tabel 1.

Table1: List of Experimental Inhibitory Zones (i.z.) of 2-amnio-arylthiazole Derivatives Against Five Types of Bacteria.

		Inhibitory zone (i.z.) diameter (mm)				
		Gram negative bacteria			Gram positive bacteria	
Molecular No.	Molecular name	Klebsiella pneumoniae	Staphylococcus aereus	Escherichia coli	Bacillus substilis	Pseudomonas areginosa
1	4-phenylthiazol-2-amine	1	1	2	1	1
2	4-(4-chlorophenyl)thiazol-2-amine	1	1	3	2	2
3	*N*-(4-phenylthiazol-2-yl)pyrrolidine-2-carboxamide	3	2	4	2	2
4	*N*-(4-(4-chlorophenyl)thiazol-2-yl)pyrrolidine-2-carboxamide	3	2	4	4	5
5	2-amino-3-phenyl-*N*-(4-phenylthiazol-2-yl)propanamide	3	2	5	2	3
6	2-amino-*N*-(4-(4-chlorophenyl)thiazol-2-yl)-3-phenylpropanamide	4	3	6	6	4
7	2-amino-3-(4-((2,6-dichlorobenzyl)oxy)phenyl)-*N*-(4-phenylthiazol-2-yl)propanamide	4	3	5	2	3
8	2-amino-*N*-(4-(4-chlorophenyl)thiazol-2-yl)-3-(4-((2,6-dichlorobenzyl)oxy)phenyl)propanamide	8	4	7	7	5
9	2-amino-3-(1*H*-indol-3-yl)-*N*-(4-phenylthiazol-2-yl)propanamide	6	4	6	3	5
10	2-amino-*N*-(4-(4-chlorophenyl)thiazol-2-yl)-3-(1*H*-indol-3-yl)propanamide	9	6	8	8	8
11	2-amino-3-(1-((benzyloxy)methyl)-1*H*-imidazol-4-yl)-*N*-(4-phenylthiazol-2-yl)propanamide	3	2	3	2	4
12	2-amino-3-(1-((benzyloxy)methyl)-1*H*-imidazol-4-yl)-*N*-(4-(4-chlorophenyl)thiazol-2-yl)propanamide	3	4	4	4	4
13	2-amino-3-(benzyloxy)-*N*-(4-phenylthiazol-2-yl)propanamide	2	2	3	2	2
14	2-amino-3-(benzyloxy)-*N*-(4-(4-chlorophenyl)thiazol-2-yl)propanamide	4	2	4	4	3
15	2-amino-5-(3-nitroguanidino)-*N*-(4-phenylthiazol-2-yl)pentanamide	3	2	4	2	3
16	2-amino-*N*-(4-(4-chlorophenyl)thiazol-2-yl)-5-(3-	6	4	5	5	5



nitroguanidino)pentanamide

Figure 1: Chemical Structures of 16 Thiazole Derivatives.

4. RESUILTS AND DISCUSSION

The derivation of theoretical molecular descriptors proceeds from the chemical structure of the compounds. The training sets of prepared molecules are summarized in Table 2. Four QSAR models for each bacteria type were produced, overall, 20 models for all bacteria types are built up using a training set of 16 molecules and parametrically depicted in Eqs. 1-20 with correlation coefficient (R^2=0.801-0.955). It is well known that a high predictive ability can be obtained when MLR model is one that has high R^2 and Fisher ratio (F) values, low standard error (S) and least number of descriptors [21,22].

Table 2: Calculated Physio-Chemical Descriptors of the Thiazole Compounds

Molecule No.	H.E.	Pol.	Mass	Ref.	Log p	Vol.	S.A.	S.G.	HOMO	LUMO	E. gap	N.E.	T.E.	D.M
1	-9.75	20.26	176.24	56.87	0.35	538.89	270.42	353.01	-8.2788	-0.1854	-8.0934	276.240	-68.709	2.183
2	-9.4	22.19	210.68	61.59	0.13	582.31	305.49	367.92	-8.3767	-0.4072	-7.9695	315.588	-81.944	3.683
3	-6.66	30.19	273.35	81.73	0.21	807.92	391.46	496.17	-8.4276	-0.3321	-8.0955	612.885	-115.165	4.773
4	-6.42	32.02	307.8	86.45	-0.02	856.18	426.84	529.12	-8.7675	-0.5477	-8.2198	662.881	-128.401	5.203
5	-10.47	36.86	323.41	102.93	0.74	929.03	428.72	555.43	-8.9754	-0.816	-8.1594	819.415	-134.982	3.017
6	-9.17	38.79	357.86	107.64	0.51	972.38	461.9	570.74	-8.8144	-0.7602	-8.0542	884.222	-148.212	2.042
7	-11.69	52.85	498.43	147.48	0.31	1267.03	562.93	699.84	-9	-0.793	-8.207	1509.675	-209.165	2.92
8	-10.51	54.78	532.87	152.2	0.09	1319.23	601.35	736.75	-8.9236	-0.8164	-8.1072	1568.075	-222.395	2.935
9	-12.9	40.92	362.45	114.22	-1.1	1002.12	431.25	582.03	-8.3744	-0.7691	-7.6053	1003.954	-152.477	3.268
10	-12.05	42.84	396.89	118.94	-1.32	1057.38	480	619.28	-8.3476	-0.6822	-7.6654	1052.557	-165.706	2.687
11	-10.67	47.99	433.53	132.87	-0.48	1168.2	499.06	635.99	-8.6678	-0.4303	-8.2375	1430.535	-188.471	3.068
12	-10.28	49.92	467.97	137.58	-0.7	1212.28	536.83	663.72	-8.3715	-0.5921	-7.7794	1505.713	-201.706	1.76
13	-12.17	39.33	353.44	109.21	0.32	1033.58	499.55	616.23	-8.5476	-0.8349	-7.7127	915.885	-152.476	2.96
14	-11.01	41.26	387.88	113.93	0.1	1069.17	522.53	640.25	-8.5086	-0.4504	-8.0582	963.045	-165.713	4.63
15	-25.85	38.18	377.42	102.14	1.08	1052.35	541.19	637.49	-8.7197	-0.5777	-8.142	1034.943	-175.713	3.713
16	-23.97	40.11	411.87	106.86	0.86	1091.79	562.02	656.7	-8.6615	-0.5768	-8.0847	1091.579	-188.949	2.642

H.E. = Hydrogen Energy(Kcal.mol^{-1}), Pol = Polarizability (A^3), Mass = Molecular mass (amu), Ref = Refractivity (A^3), Vol. = Volume (A^3), S.A. = Surface area-Appro (A^2), S.G = Surface Area-Grid (A^2), HOMO = HOMO Energy level (eV), LUMO = LUMO Energy level (eV), E.gap = Energy gap (eV), N.E = Nuclear Energy (Hartree) T.E. = Total Energy (Hartree), D.M. = Dipole Moment (Debyes).

Eq. 1-4 gave correlation of parametric descriptors of thiazole derivatives with inhibitory zones of Pseudomonas areginosa. The number of descriptors is generally modified with an increase of correlation coefficient. It's clearly seen that Eq. 1 is influenced by four descriptors, Log p, HOMO, N.E., and T.E. In addition, the correlation coefficient value of this model is 0.806. While, Eq. 2 and Eq.3 depend on five descriptors which gives model with higher correlation coefficient, R^2= 0.906 and 0.92, respectively.

i.z. = -2.8419 Log p-3.4188 HOMO-0.0119 N.E-0.1117 T.E.-31.2879 (1)

n=16, R^2=0.806, F= 11.477, S=0.873

i.z. = -0.5004 Pol.-4.9574 Log p+0.0453 S.A.-8.9095 HOMO-0.7735 D.M.-64.8516 (2)

n=16, R^2=0.906, F=19.344, S=0.637

i.z. = -0.1627 Ref-4.9139 Log p+0.0397 S.A.-8.186 HOMO-0.798 D.M.-64.9613 (3)

n=16, R^2=0.92, F= 23.019, S= 0.589

According to these equations, positive values of parameters refer to positive relationship, while negative parameters values refer to reversible relationship [23], Compared with Eq. 1-3, the robust model with correlation coefficient (R^2=0.955) can be found in Eq. 4., and statistical data R^2, F and S were improved by using six descriptors, Ref, Log p, HOMO, N.E., T.E., and D.M. The statistical procedure known as linear regression basically involves drawing and analyzing trend-lines through data points, which are experimental and calculated data [24], as plotted in Figure.2. This model is validity to establish antibacterial activities for predicted molecules.

i.z. = -0.1053 Ref-4.1055 Log p-6.6947 HOMO-0.011 N.E.-0.1516 T.E.-0.6691 D.M.-53.0278 (4)

n=16, R^2=0.955, F=32.023, S=0.464

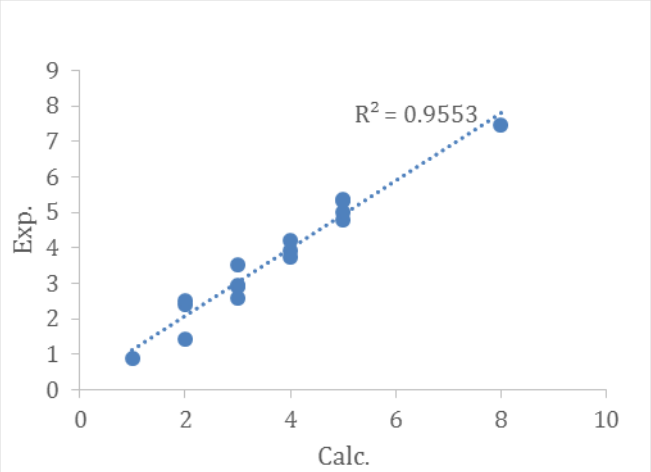


Figure 2: Experimental i.z. vs. Predicted i.z. Calculated By Eq. 4

Correlation of inhibitory zone of next gram positive bacteria, Bacillus substilis, with thiazole parametric descriptors was also found and depicted in Eq. 5-8. The Eq. 5 needed five descriptors to build model with correlation coefficient value R^2=0.817, while, Eq. 6 and Eq. 7 needed six descriptors to build better models with regression coefficient, about R^2=0.824 and R^2=0.884, respectively. Well-founded model interrelationship between antibacterial activity and other parameters goes to Eq. 8 with R^2=0.915. Good relationship between the experimental data and predicted antibacterial activities was illustrated as trend-line in Figure.3.

i.z. = 0.2419 H.E.-1.761 Log P-0.0263 N.E.-1.2039 T.E.-3.8021 D.M.+8.9435 (5)

n=16, R^2=0.817, F=8.943, S=1.18

i.z. = 0.1986 Mass-0.3691 Ref-1.8126 Log p+0.0563 S.G.+0.339 T.E.-1.0465 D.M-5.9672 (6)

n=16, R^2=0.824, F=7.024, S=1.08

i.z. = 0.2186 H.E-3.0612 Log P-4.622 E.gap-0.0313 N.E-0.2939 T.E.-1.6282 D.M.-40.77133 (7)

n=16, R^2=0.887, F=11.882, S=0.89

i.z. = 2.6578 Pol.+0.0734 Mass-0.7839 Ref-2.8401 Log P-4.626 E.gap-0.0296 N.E.-1.5777 D.M.- 45.7739 (8)

n=16, R^2=0.915, F=12.408, S=0.82

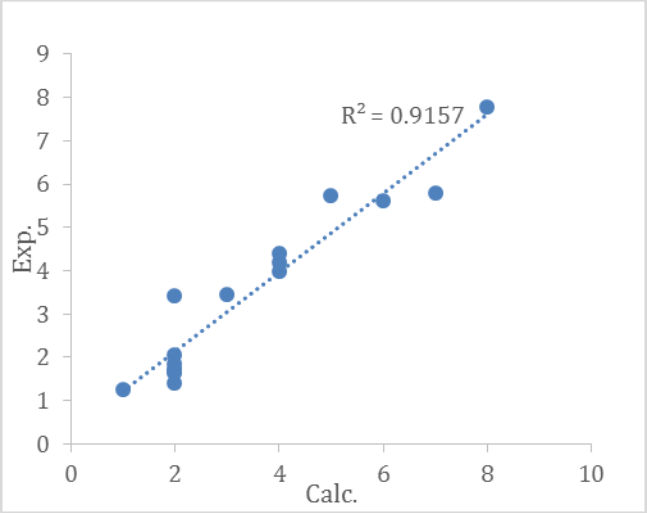


Figure 3: Experimental i.z. vs. Predicted i.z. Calculated By Eq. 8

On the other hand, the inhibitory zone of Staphylococcus aereus, gram negative bacteria, by thiazoles was analytically regressed to generate Eq. 9-12. Fairly good correlation coefficients were obtained with least number of descriptors, R^2=0.855, 0.889, 0.892 for Eq. 9, Eq. 10, and Eq. 11, respectively. Although of those good interrelationships, but parametric model was developed to get better results. Eq. 12 is the best predicated which depends on only 6 parameters, and it also provides good model with correlation coefficient, R^2= 0.954. Figure.4 shows graph of experimental and predicted data obtained by Eq. 12.

i.z. = -1.5409 Log p-0.009 N.E-0.0927 T.E-0.6041 D.M.- 0.8647 (9)

n=16, R^2=0.855, F=16.336, S=0.59

i.z. = 0.02803 Mass-1.4328 Log p-0.0351 Vol+0.5815 S.G.-0.5815 D.M.-1.262 (10) 10

n=16, R^2=0.889, F=15.685, S=0.55

i.z. = 3.8833 Pol-0.8946 Ref-0.0925 Vol+0.0709 S.G.+3.346 E.gap+24.7004 (11)

n=16, R^2=0.892, F=16.586, S=0.53

i.z. = 2.9591 Pol-0.687 Ref-1.0827 Log p-0.086 Vol+0.087 S.G.-0.6595 D.M.-1.9898 (12)

n=16, R^2=0.954, F=31.531, S=0.36

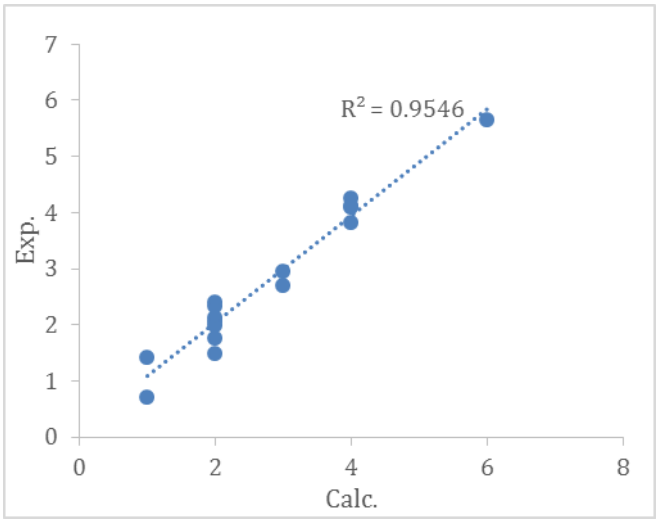


Figure 4: Experimental i.z. vs. Predicted i.z. Calculated By Eq. 12

Attempting to fit models correlate thialzole structure and inhibitory zone against Escherichia coli bacteria were statistically generated in Eq. 13-16. There is a significant relationship fitted on Eq. 16 mutually related with seven descriptors, and its correlation coefficient value was 0.918, which modeled and plotted as line-graph in Figure 5. Other models give the least correlation coefficient values, R^2=0.899 for Eq. 15, R^2=0.862 for Eq. 14, and R^2=0.819 for Eq. 13.

i.z. = 0.4.5139 Pol-0.8528 Ref-0.1614 Vol+0.1459 S.G.-4.7032 (13)

n=16, R^2=0.819, F=12.51, S=0.78

i.z. = -0.6688 H.E.+8.3923 Pol+0.267 Mass-2.492 Ref+0.9326 T.E-15.5742 (14)

n=16, R^2=0.862, F=12.558, S=0.71

i.z. = -0.2533 H.E.+6.843 Pol-1.4479 Ref-0.0735 Vol-0.0735 N.E.-9.7352 (15)

n=16, R^2=0.899, F=17.874, S=0.61

i.z. = -0.2195 H.E.+7.1124 Pol-1.5494 Ref-0.0708 Vol-0.0292 N.E.-0.1368 D.M.-9.33 (16)

n=16, R^2=0.918, F=16.95, S=0.58

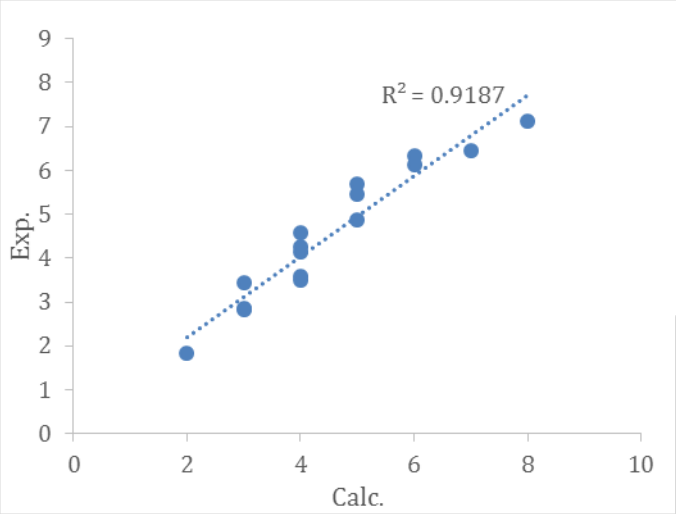


Figure 5: Experimental i.z. vs. Predicted i.z. Calculated By Eq. 16

Analysis of synthesized thiazole derivatives as antibacterial activities against Klebsiella pneumoniae bacteria was regressed. As a result, three first models represented in Eq. 17-19 have correlation coefficient values 0.884, 0.855, and 0.815, respectively. While, the last one, Eq. 20, shows excellent relationship to estimate activity that was achieved mathematically by seven parameters, and has good correlation coefficient value, R^2=0.902. Best-fit line was created and drown in Figure 6 using both experimental and calculated variables of the last model.

i.z. = 0.1089 Mass-0.0935 Vol-0.0915 S.A.+0.1846 S.G.-7.7845 (17)

n=16, R^2=0.815, F=12.116, S=1.13

i.z. = 0.0978 Mass-1.0218 Log p-0.0898 Vol-0.063 S.A.+0.1622 S.G.-7.5626 (18)

n=16, R^2=0.855, F=6.719, S=1.05

i.z. = 0.0169 Mass-0.3762 Ref-0.1616 S.A.+0.1404 S.G.-0.0144 N.E.-0.7148 D.M.-7.4443 (19)

n=16, R^2=0.8843, F=11.47, S=0.99

i.z. = 0.1681 Mass-0.3461 Ref-0.1513 S.A.+0.1317 S.G.+1.584 HOMO-0.0155 N.E.-0.6542 D.M.+4.727 (20)

n=16, R^2=0.902 F=10.57, S=0.96

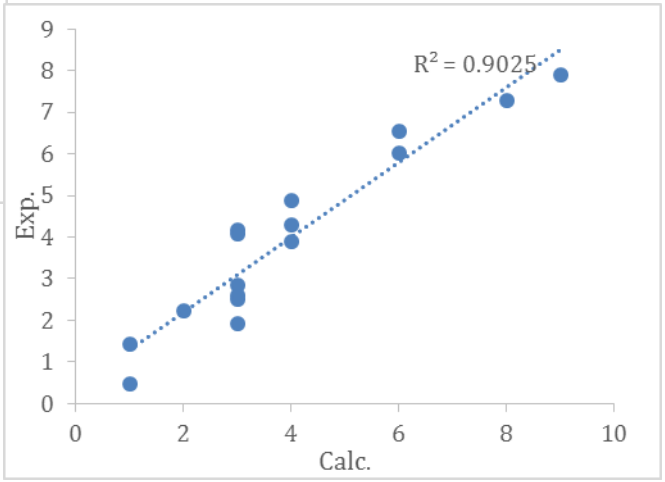


Figure 6: Experimental i.z. vs. Predicted i.z. Calculated By Eq. 20

A reliable equation, i.e. only high correlation coefficient (R^2>9) equation, was used dependably to predict antibacterial activities of other 15 designed and unprepared conjugated thiazole-amino acids, numbered 17-31, as shown in Figure 7. Theoretical physio-chemical descriptors for proposed and untested molecules were determined and

listed in Table 3. Then, they were applied statistically in Eq. 4, Eq. 8, Eq. 12, Eq. 16, and Eq. 20 to calculate their inhibitory zones as predictable results. By observation of calculated results in table 4, it can be seen that compounds no. 28 and 29 show good antibacterial activity against Klebsiella pneumoniae, with 9.7 mm and 9.2 mm i.z., respectively. Two compounds, no. 18 and 29, can easily observe that higher inhibitory zones against Staphylococcus aereus, and five of the 15 designed molecules gave best antibacterial activities against Escherichia coli, in particular, 22.6 mm i.z. by no. 18 and 22.7 i.z. mm by no. 29. Most of the predicted compounds exhibited good results against gram positive bacteria. For example, 13.5 mm i.z. of Bacillus substilis with compound no. 25 and 15.9 mm i.z. of Pseudomonas areginosa with compound no. 28.

Table 3: Calculated Physio-Chemical Descriptors of the Proposed Compounds

Molecule No.	H.E.	Pol.	Mass	Ref.	Log p	Vol.	S.A.	S.G.	HOMO	LUMO	E. gap	N.E.	T.E.	D.M
17	-11.18	27.29	267.73	74.39	-0.95	732.52	387.99	461.7	-8.6424	-0.5321	-8.1103	496.54	-112.26	1.932
18	-9.72	29.13	281.76	68.21	2.17	779.26	413.14	481.98	-8.6669	-0.5231	-8.1438	555.44	-117.98	2.043
19	-8.09	32.8	309.81	87.88	0.46	864.84	446.52	521.8	-8.6237	-0.487	-8.1367	686.47	-129.43	3.429
20	-7.67	34.63	323.84	92.56	0.79	921.65	491.8	558.99	-8.6561	-0.5089	-8.1472	749.00	-135.15	3.151
21	-7.53	34.63	323.84	92.48	0.86	913.45	476.34	546.43	-8.6222	-0.4838	-8.1384	751.13	-135.15	3.469
22	-13.92	29.76	297.76	80.43	-1.19	800.49	408.24	496.19	-8.5531	-0.4671	-8.086	620.24	-129.77	3.234
23	-12.31	31.6	311.79	84.85	-0.78	838.69	421	514.33	-8.5114	-0.4865	-8.0249	689.72	-135.49	3.331
24	-10.86	32.13	313.82	86.55	-0.61	824.72	425.34	510.87	-8.5561	-0.5375	-8.0186	614.74	-125.12	3.929
25	-9.44	35.8	341.87	96.22	-0.42	937.17	505.49	570.7	-8.6981	-0.6033	-8.0948	737.20	-136.57	1.486
26	-13.86	35.98	338.85	96.2	-0.64	972.52	509	590.02	-8.6951	-0.5803	-8.1148	803.37	-143.27	1.803
27	-21.01	38.27	366.87	101.89	-0.81	1028.22	502.8	622.91	-8.5471	-0.4201	-8.127	925.77	-158.45	5.008
28	-12.5	34.12	333.8	93.22	-2.22	864.4	372.11	511.42	-8.9827	-1.0346	-7.9481	803.21	-142.54	4.897
29	-16.58	31.69	325.77	74.25	1.55	847.62	436.28	525.88	-8.5396	-0.5194	-8.0202	731.12	-146.26	4.595
30	-15.29	33.52	339.8	89.67	-0.78	909.6	481.08	558.28	-8.7248	-0.6027	-8.1221	783.53	-151.98	2.465
31	-14.99	32.4	324.78	86.74	-1.89	863.23	428.84	531.44	-8.5166	-0.4188	-8.0978	731.69	-142.59	6.274

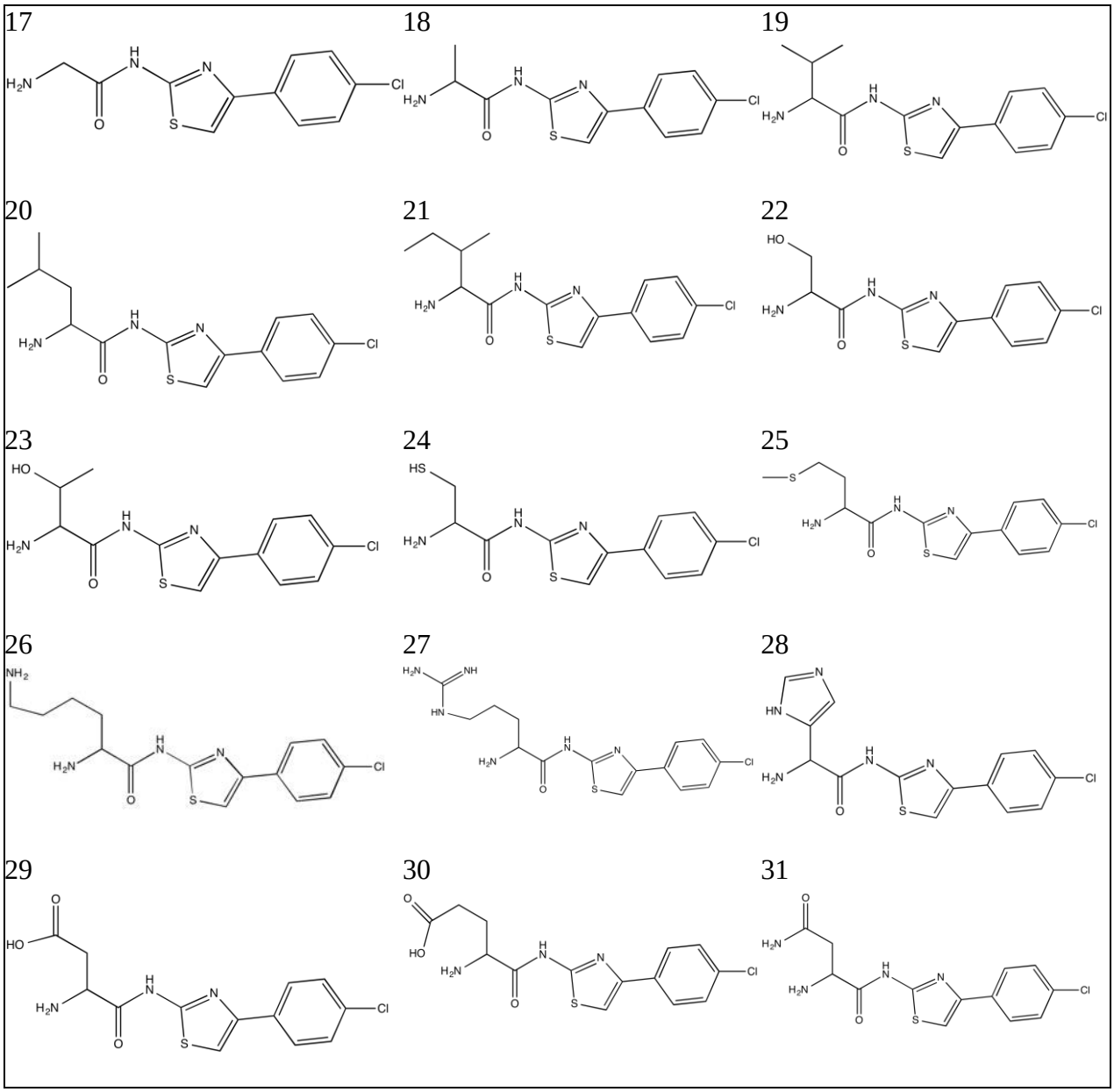


Figure 7: Chemical Structures of Proposed Thiazole Derivatives

Table 4: List Of Predicted Inhibitory Zones (i.z.) of Proposed Thiazole Derivatives Against Five Type of Bacteria.

Molecular No.	Molecular name	Calculated inhibitory zone diameter (mm)				
		Gram negative bacteria			Gram positive bacteria	
		Klebsiella pneumoniae	Staphylococcus aereus	Escherichia coli	Bacillus substilis	Pseudomonas areginosa
17	2-amino-*N*-(4-(4-chlorophenyl)thiazol-2-yl)acetamide	3.4	4.6	5.3	10.6	11.2
18	2-amino-*N*-(4-(4-chlorophenyl)thiazol-2-yl)propanamide	5.8	8.6	22.6	10.7	-0.7
19	2-amino-*N*-(4-(4-chlorophenyl)thiazol-2-yl)-3-methylbutanamide	1.0	3.0	7.8	5.9	3.3
20	2-amino-*N*-(4-(4-chlorophenyl)thiazol-2-yl)-4-methylpentanamide	-0.9	3.3	7.7	5.8	2.1
21	2-amino-*N*-(4-(4-chlorophenyl)thiazol-2-yl)-3-methylpentanamide	-0.5	2.7	8.3	5.0	1.3
22	2-amino-*N*-(4-(4-chlorophenyl)thiazol-2-yl)-3-hydroxypropanamide	5.2	4.3	5.5	9.5	11.3
23	2-amino-*N*-(4-(4-chlorophenyl)thiazol-2-yl)-3-hydroxybutanamide	5.5	4.5	6.7	8.3	8.9
24	2-amino-*N*-(4-(4-chlorophenyl)thiazol-2-yl)-3-mercaptopropanamide	4.8	5.2	10.6	9.2	7.2
25	2-amino-*N*-(4-(4-chlorophenyl)thiazol-2-yl)-4-(methylthio)butanamide	1.4	6.4	10.2	13.5	8.4
26	2,6-diamino-*N*-(4-(4-chlorophenyl)thiazol-2-yl)hexanamide	1.7	5.6	8.0	12.0	9.4
27	2-amino-*N*-(4-(4-chlorophenyl)thiazol-2-yl)-5-guanidinopentanamide	5.9	4.6	9.1	7.6	7.3
28	2-amino-*N*-(4-(4-chlorophenyl)thiazol-2-yl)-2-(1*H*-imidazol-5-yl)acetamide	9.7	4.3	6.3	7.9	15.9
29	3-amino-4-((4-(4-chlorophenyl)thiazol-2-yl)amino)-4-oxobutanoic acid	9.2	8.9	22.7	8.0	1.0
30	4-amino-5-((4-(4-chlorophenyl)thiazol-2-yl)amino)-5-oxopentanoic acid	4.0	5.2	5.9	10.7	11.9
31	2-amino-N^1-(4-(4-chlorophenyl)thiazol-2-yl)succinamide	5.5	4.2	6.7	7.5	12.0

5. CONCLUSION

The models of QSAR study of 16 derivatives of amino acids conjugated 2-amnio-arylthiazole were successfully investigated as *in vitro* anti-bacteria. By using MLR method with help of the numerous descriptors, it can correlate with experimental inhibitory zones of bacteria. Five excellent models with high correlation coefficient, high fisher ratio, and low standard error have been built. QSAR studies indicated that strong relationship between (Ref., Log p, HOMO, N.E, T.E., and D.M.) and inhibitory zone of Pseudomonas areginosa was found in Eq. 4 with R^2=0.955. Also, Eq. 8 with R^2=0.915 was found to contribute to antibacterial activity against Bacillus substilis which depend on parameters (Pol., mass, Ref., Log P, E. gap, N.E, and D.M.). Further, (Pol., Ref, Log p, Vol., S.G., and D.M.) were the key properties for explaining thiazole anti-Staphylococcus aereus activity which was achieved in Eq. 12 with R^2=0.954. Statistical significance in the screening best equation to calculate predictably anti-Escherichia coli was directly influenced on descriptors (H.E., Pol., Ref, Vol., N.E., and D.M.), and

founded in Eq. 16 with R^2=0.918. In addition, anti-Staphylococcus aereus was well linked with parameters (Mass., Ref., S.A., S.G., Homo, N.E. and D.M.) in Eq. 20 with R^2=0.902. Proposing more thiazole derivatives gives subset of variables are more effective as anti-bacteria. Good results of new untested-set evaluated at Eq. 4, Eq. 8, Eq.12, Eq.16, and Eq. 20, which showed most of them good inhibitors for gram positive of bacteria.

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دراسات علاقة التركيب-الفعالية الكمية للأحماض الأمينية المقترنة مع مركب ٢-امينوارايل ثايوزول كمضاد للبكتريا

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المستخلص

تم في هذا البحث دراسة علاقات التركيبية الفعالية الكمية (QSAR) الى ستة عشر مشتق من مركبات الثايوزول كمضاد بكتريا (Klebsiella pneumonia و Staphylococcus aereus و Escherichia coli و Bacillus substilis و Pseudomonas areginosa) ، حيث تم الحصول على المتغيرات الفيز-كيمياوية حسابياُ للتراكيب الكيميائية لمشتقات الثايوزول باستخدام طريقة ميكانيك الكم (MM+) وكذلك طريقه شبه التجريبية (AM_1) عند الطاقة الدنيا للمركبات ، ثم أنجزت المعادلات التي تربط الصفات التركيبية للمشتقات الثايوزول مع فعاليتها كمضاد للبكتريا باستخدام التحليل الخطي المتعدد الارتداد ، حيث تم استنتاج ٢٠ موديل يتراوح معاملها الارتباط R^2 بين (0.806-0.955) واستخدمت بعدها اعلى قيمة ارتباط (R^2>0.9) للتنبؤ بفعالية كمضاد للبكتريا الى خمسة عشر مركب مفترض من الاحماض الامينية المقترنة مع ٢-امينوارايل ثايازول ، واظهرت النتائج ان معظم المركبات المفترضة لها فعالية جيده ضد بكتريا كرام الموجبة.