

Supporting information for

Antimicrobial Pharmacophore Screening of Imidazole[1,2-a] Pyrazine Derivatives: A Quantitative Structure-Activity Relationship Approach

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DOI: <http://dx.doi.org/10.30919/cs1449>

Table S1: Theoretical prediction of ADME properties of the studied compounds.

Molecules	MW	H-bond acceptors	H-bond	Rotatable	Molar	Lipophilicity
			donors	bonds	refractivity	
1(A)	311.34	4	1	4	91.01	3.48
2(B)	281.36	2	2	3	86.59	2.97
3(C)	255.23	4	1	2	71.65	1.84
4(D)	225.25	2	2	1	67.23	1.33
5(E)	311.34	4	1	4	91.01	3.48
6(F)	281.36	2	2	3	86.59	2.97
7(G)	337.38	4	1	4	98.47	4.31
8(H)	225.25	2	2	1	67.23	1.33
9(I)	309.41	2	1	4	96.39	3.78
10(J)	253.3	2	1	2	77.03	2.13

Table S2: Statistical validation of the GA-MLR model.

Model	R ² _Train	R ² _Test	RMSE_Train	RMSE_Test	R ² _Adjusted
GA-MLR	0.9150714	0.2291822	0.1858331	3.014309	0.4054999

Lack_of_Fit	F_Value	CV_R ²	CV_RMSE	Intercept	Q ²
0.2532489	1.795767	0.8231608	1,076.319	1.534504	-5.861005

Q ² _loo	Y_Scrambling_Mean	Y_Scrambling_SD
0.9150714	1	0.0000000000000001115816

Table S3: Validation criteria.

R^2_{train}	R^2_{adj}	$R^2_{R^2\text{adj}}$	LOF
0.9150714	0.4054999	0.5095715	0.2532489

Kxx	Delta_K	RMSE_tr	MAE_tr
0.5032384	2	0.1858331	0.1416266

RSS_tr	CCC_tr	s	F
0.7597468	0.9556525	0.5032384	1.795767

Q^2_{loo}	$R^2_{Q^2\text{loo}}$	RMSE_cv	MAE_cv
0.9150714	-0.0000000000000001110223	1,076.319	0.1416266

PRESS_cv	CCC_cv	$Q^2\text{LMO}$	R^2Y_{scr}
0.7597468	0.9556525	-5.861005	1

Q^2Y_{scr}	RMSE_AV_Yscr	R^2X_{rnd}	Q^2X_{rnd}
1	0.0000000000000001115816	1	1

R^2Y_{rnd}	Q^2Y_{rnd}	RMSE_ext	MAE_ext
1	1	3.014309	1.579153

PRESS_ext	R^2_{ext}	Q^2_{F1}	$Q^2_{F^2}$
63.6024	0.2291822	-5.228338	-5.861005

Q ² _F ³	CCC_ext	r ² m_aver	r ² m_delta
-5.228338	-0.3478359	-2.815911	6.090187

Table. S4: Virtual screening of molecules based on activity model data.

Molecule_ID	final_response	Rank
8	0.02924920	1
3	0.09303062	2
4	0.12321198	3
10	2.30315848	4
6	5.73753726	5
5	5.85973614	6
1	8.60595267	7
2	23.46013693	8
7	26.79833894	9
9	82.17119809	10
NB: Values are as per the activity units (µg/mL)		

Table S5: Binding free energy components for the Staphylococcus aureus Pyruvate Carboxylase bound to MOLECULE 8 calculated by MM-GBSA.

Energies (kcal/mol)	Staphylococcus aureus Pyruvate Carboxylase bound to MOLECULE
	8
ΔG_{bind}	-68.86
$\Delta G_{\text{bindLipo}}$	-21.91
$\Delta G_{\text{bindvdW}}$	-34.45
$\Delta G_{\text{bindCoulomb}}$	31.65
$\Delta G_{\text{bindHbond}}$	-4.01
$\Delta G_{\text{bindSolvGB}}$	43.81
$\Delta G_{\text{bindCovalent}}$	3.19
$\Delta G_{\text{bindPacking}}$	-5.42

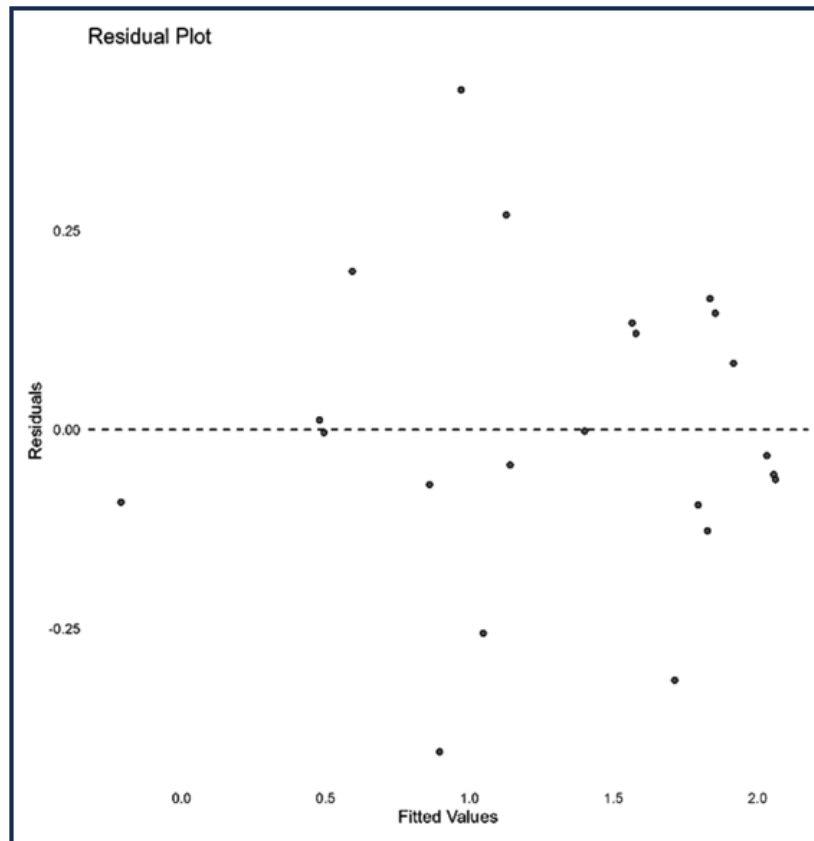


Fig. S1: Residual plot showing the residuals versus fitted values.

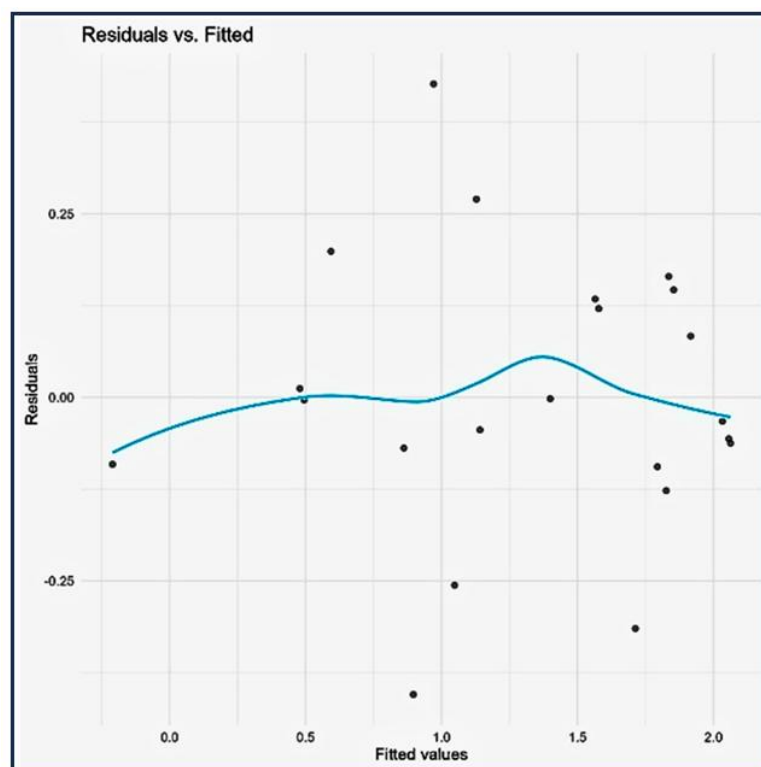


Fig. S2: Plot showing residuals versus fitted values.

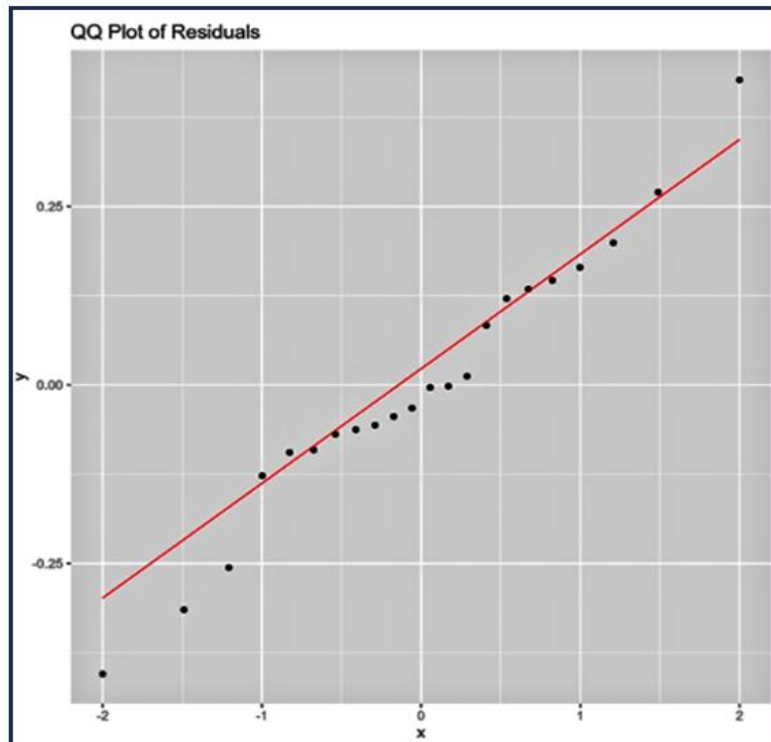


Fig. S3: QQ plot of residuals to check the normality assumption.

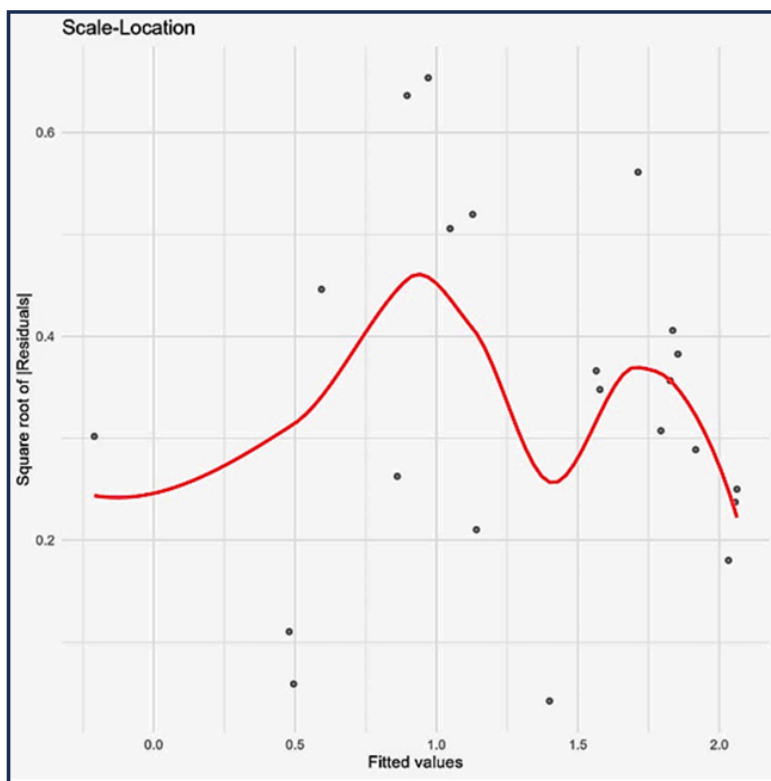


Fig. S4: Scale-Location plot showing the spread of residuals.

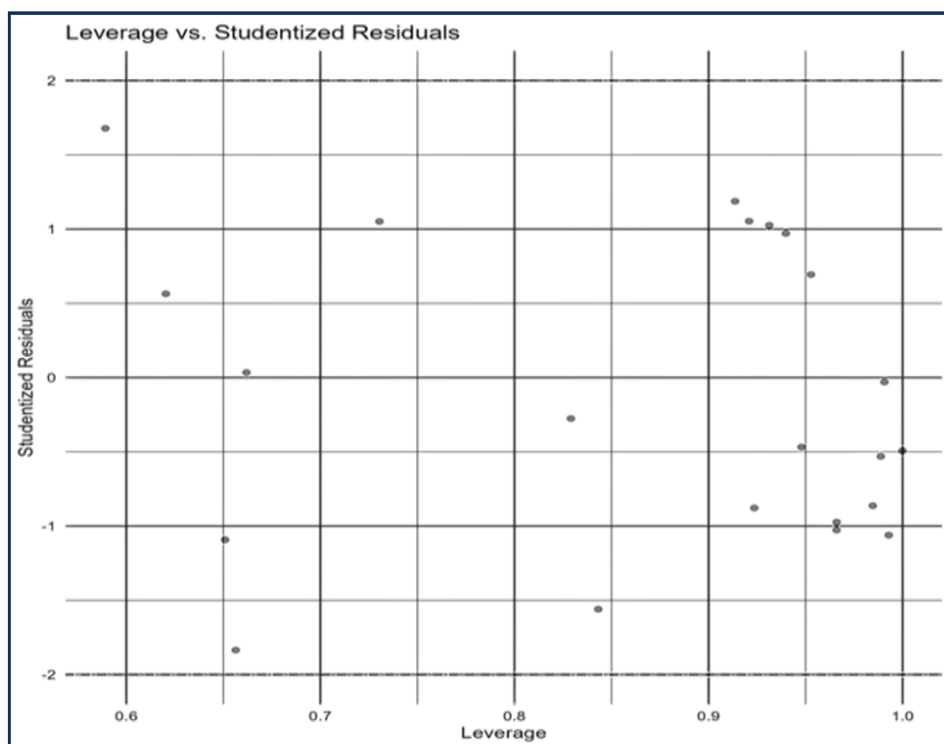


Fig. S5: Plot showing leverage versus studentized residuals.

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