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Antimicrobial activity analysis and QSAR studies of p-coumaric Acid derivatives using physicochemical parameters

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ABSTRACT

A Quantative-Structure-Activity Relationship (QSAR) study is performed on set of 36 p-cumaric Acid derivatives and number of highly descriptive and predictive QSAR models for these compounds were obtained by Using physicochemical parameters using stepwise-multiple linear regressions methods.. Model validation is performed by incorporating training and test sets approach and calculating R^2 which is equal to 0.5979 and also Regression analysis data has indicated that activity can be best modeled in multi-parametric regression.

Keywords: p-coumaric Acid derivatives, QSAR, Molar Volume, Molar Refractivity, Parachore, Density, Refractive Index, Surface Tension, Polarizability

INTRODUCTION:

Development of new and different antimicrobial drugs is an important objective and much of research program efforts are directed towards the design of new agents, the reason being that the usage of most antimicrobial agents is limited, not only by the rapidly developing drug resistance, but also by unsatisfactory status of present treatment of bacterial and fungal infections and drug side effects [1-3]. Some substituted anilides, which very recently appeared in literature, have received considerable attention due to their wide range of biological activities *viz*. antibacterial, antifungal, anticonvulsant, anaesthetic, antiproliferative, antiplaque, antiplatelet-aggregation, antioxidant and potassium channel activating potentials [4-13].

QSAR analysis is a widely used statistical methods to describe the relationship between chemical structure and biological activities of a series of analogs quantitatively [14]. In view of the above and in continuation to our work on QSAR studies in describing the biological activity [15-22], in the present study we report the QSAR studies of p-coumaric acid derivatives using physicochemical parameters.

Experimental Details

For QSAR study MIC values in µg/ml were transformed into pMIC values.(i.e. –log MIC in µg/ml) which are reported in table A-I

Parameters used

We have used following physicochemical parameters for modeling of $pMIC_{ab}$ and $pMIC_{am}$ of various pCoumaric acid derivatives which were calculated by using ACD labs software Chemsketch[14].

(1)Molecular volume (MV)

$$MV = \frac{MW}{d}$$

(2) Molar refractivity (MR)

$$MR = \frac{n^2-1}{n^2+2}.\frac{MW}{d}$$

(3) Parachor (P)

$$P_r = \left(\frac{MW}{d}\right)\gamma^{1/4}$$

(4) Density (d)

$$d = \frac{MW}{MV}$$

(5) Refractive Index(n)

$$n = \sqrt{\frac{2MR+MV}{MV-MR}}$$

(6) Surface tension (γ)

$$\gamma = \left(\frac{P_r}{MV}\right)^4$$

(7) Polarizability (α)

Polarizability=0.3964308.MR

The compounds used in the present study with their values are reported in Table A-I, The values of various parameters obtained are reported in Table A-II.

Results and Discussion:

A} Modeling $pMIC_{ab}$ using Physicochemical parameters

A close look of table A-III revels that
1) Out of Eight mono-parametric model,MW shows the highest regression value for the best model.
2) Out of ten bi-parametric model,MR and D together shows the highest regression value for the best model.
3) Out of ten tri-parametric model,MR,D and POL together shows the highest regression value for the best model.
4) Out of ten tetra-parametric model,MR,MV,IR and D together shows the highest regression value for the best model.

Mono-Parametric model

$pMIC_{ab} = 0.0032(\pm0.0005)MW + 0.4857$ (A-1)
$N= 37, R^2 =0.5545, R^2A=0.5414, Se= 0.0810, F=42.3120$

When MR and D were taken together a bi-Parametric model has been obtained with improved statistics here R^2 comes out to be 0.5855.

Bi-Parametric model

$pMIC_{ab} = 0.0092(\pm0.0018)MR + 0.3638 (\pm0.1593)D +0.1743$
(A-2)
$N=37, R^2 = 0.5855, R^2A = 0.5604, Se=0. 0793, F=23.3110$

A tri-Parametric model has been obtained when MR, D and POL were taken together. In this model the R^2 shows significant improvement.

Tri-Parametric model

$pMIC_{ab} = 1.5411(\pm2.2556)MR + 0.3705(\pm0.1609)D$
$-3.8647(\pm5.6900)POL + 0.1586$ (A-3)
$N=37, R^2 = 0.5914, R^2A = 0.5531, Se= 0.0799, F= 15.4410$

A tertra-parametric model has been obtained when MR,MV,IR and D were taken together. In this model the R^2 shows significant improvement.

Tetra-Parametric model

However very small improvement is observed in a tetra-parametric model when MR, MV, IR and D have been taken as correlating parameter. This model has been found to be excellent for modeling activity of the compounds of the present study.

$pMIC_{ab}$=0.0355(±0.0277)MR-0.0088(±0.0093)MV-2.6994(±2.7679)IR+ 0.4522(±0.3316)D + 4.3574 (A-4)

N=37, R^2 = 0.5979, R^2A =0.5460 ,Se= 0.0806, F =11.5230

Validation of model

The model has been validated by plotting a graph actual and predicted value of pMICab activity as recorded in Table A-IV obtained from tetra- parametric model.

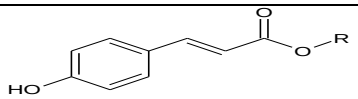
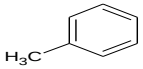
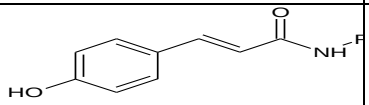
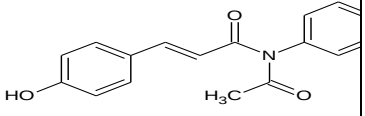
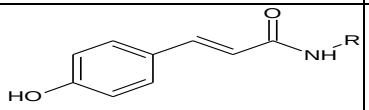
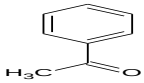
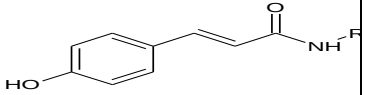
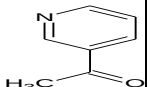
Cross- validated parameters

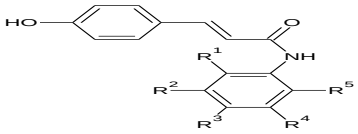
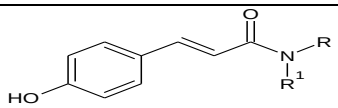
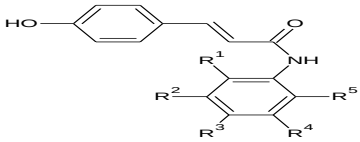
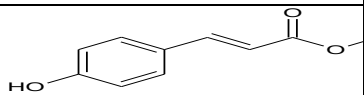
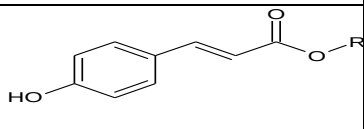
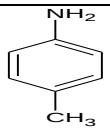
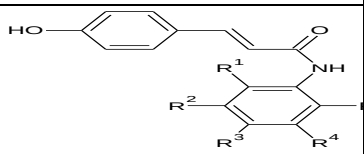
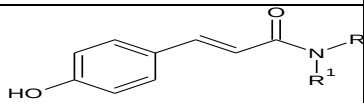
In this we observed the parameter with the high regression value which will obtained the best result.

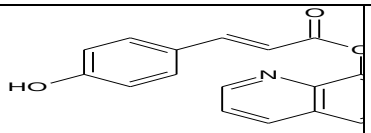
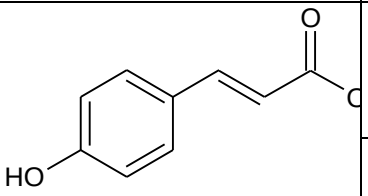
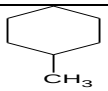
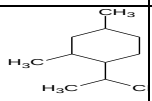
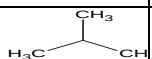
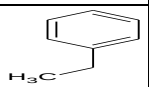
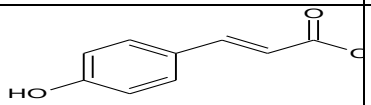
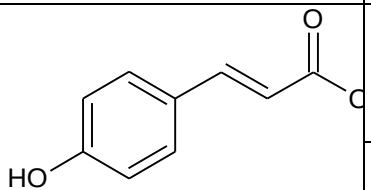
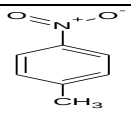
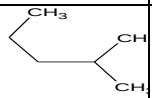
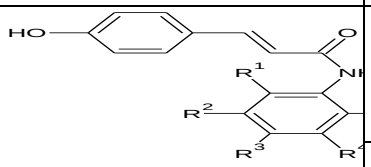
We have estimated $pMIC_{ab}$ values using Model-29. The predictive power of best Model has been obtained by plotting graph between actual and predicted $pMIC_{ab}$ values demonstrated in Fig. (a).

This clearly indicates that this is best model for estimating predicting $pMIC_{ab}$ values of the compounds in the present study.

Table A-I Structural details of compounds under study.

S. No.	Parent structure	R	R_1	R_2	R_3	R_4			$pMIC_{ab}$	$pMIC_{am}$
1.			-	-	-	-			1.08	1.16
2.		C_6H_{13}	-	-	-	-			1.40	1.36
3.		-	-	-	-	-			1.35	1.35
4.			-	-	-	-			1.23	1.27
5.			-	-	-	-			1.53	1.39

6.		H	Cl	NO_2	H	H			1.61	1.53
7.		OCH_3	H	H	H	H			1.43	1.33
8.		C_2H_4OH	C_2H_4OH						1.40	1.36
9.		-	NO_2	H	H	H			1.36	1.42
10		C_3H_7	-	-	-	-			1.22	1.16
11			-	-	-	-			1.31	1.31
12		-	H	Cl	Cl	H			1.39	1.33
13		-	H	H	NO_2	H			1.36	1.30
14		-	CH_3	H	H	NO_2			1.28	1.32
15		-	NH_2	H	H	H			1.31	1.25
16		C_4H_9	C_4H_9	-	-	-			1.24	1.22

17		-	-	-	-	-			1.67	1.73
18			-	-	-	-			1.19	1.17
19		C_4H_9	-	-	-	-			1.15	1.13
20			-	-	-	-			1.38	1.44
21			-	-	-	-			1.12	1.10
22			-	-	-	-			1.21	1.19
23		C_2H_5	-	-	-	-			1.19	1.19
24		CH_3	-	-	-	-			1.15	1.15
25			-	-	-	-			1.36	1.30
26			-	-	-	-			1.17	1.21
27		-	H	N C_2	H	H			1.26	1.30
28		-	H	H	Cl	H			1.4	1.3

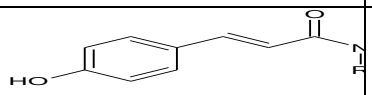
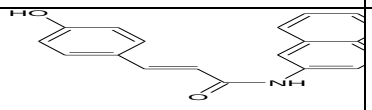
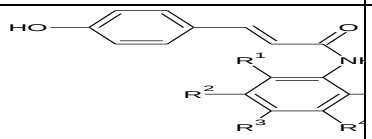
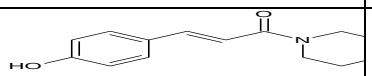
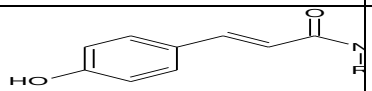
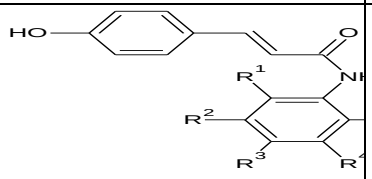
									4	4
29		C_6H_5	C_6H_5						1.60	1.46
30		-	-	-	-	-			1.46	1.24
31		-	Cl	H	NO_2	H			1.51	1.41
32		-	H	Cl	H	H			1.54	1.40
33		-	H	H	H	H			1.38	1.28
34		-	-	-	-	-			1.17	1.15
35		CH_3	CH_3						0.98	1.06
36		-	CH_3	H	CH_3	H			1.33	1.27

Table A-II Values of the calculated physicochemical parameters used in the present study

Compd. Name	**MW**	**MR**	**MV**	**PC**	**IR**	**ST**	**D**	**POL**
1	240.253	70.300	194.300	522.300	1.643	52.100	1.236	27.87
2	247.332	75.440	233.800	596.900	1.558	42.400	1.057	29.900
3	281.306	82.600	221.900	612.500	1.666	57.900	1.267	32.740
4	267.279	77.240	210.600	578.700	1.654	56.900	1.268	30.620
5	268.2	75.33	203.9	572.9	1.660	62.30	1.315	29.86

	67	0	00	00		0		0
6	318.712	84.670	213.5000	615.8000	1.723	69.1000	1.4922	33.5600
7	269.2955	79.9100	213.8000	581.2000	1.670	54.6000	1.2559	31.6700
8	251.2778	69.3700	194.2000	548.5000	1.633	63.6000	1.2933	27.5000
9	284.2676	79.7700	201.6000	580.0000	1.721	68.4000	1.4009	31.6200
10	206.2388	59.6900	181.8000	469.3000	1.570	44.3000	1.1334	23.6600
11	255.2669	74.5300	196.6000	548.1000	1.682	60.3000	1.2988	29.5400

12	308.159	83.020	213.7000	596.2000	1.704	60.6000	1.4411	32.9100
13	284.2677	79.7700	201.6000	580.0000	1.721	68.4000	1.4099	31.6200
14	298.2933	84.6000	217.9000	617.6000	1.704	64.5000	1.3688	33.5300
15	254.2844	77.4700	192.0000	550.3000	1.740	67.3000	1.3233	30.7100
16	275.3866	84.8330	265.2000	674.2000	1.552	41.7000	1.0388	33.6330
17	291.3013	86.2300	221.6000	620.2000	1.705	61.2000	1.3133	34.1800
18	24	69	21	56	1.	47	1.	27

	6.302	.650	3.200	1.000	566	.800	150	.610
19	220.264	64.330	198.300	509.100	1.562	43.400	1.110	25.500
20	302.408	88.110	280.100	715.200	1.541	42.400	1.070	34.920
21	206.238	59.650	182.200	466.700	1.568	43.000	1.131	23.640
22	254.281	74.910	209.500	561.900	1.633	51.700	1.213	29.700
23	192.211	55.060	165.300	429.500	1.580	45.500	1.162	21.820
24	178.	50.4	148.	389.	1.59	47.0	1.19	19.9

	185	30	8000	700	2	00	7	90
25	285.2522	76.8400	206.1000	577.7000	1.668	61.6000	1.383	30.4600
26	234.2911	68.9200	215.2000	546.2000	1.553	41.5000	1.088	27.3200
27	284.2667	79.7700	201.6000	580.0000	1.721	68.4000	1.409	31.6200
28	273.7144	78.1200	201.7000	560.4000	1.701	59.5000	1.356	30.9700
29	315.3665	97.7000	254.9000	702.1000	1.692	57.5000	1.237	38.7300
30	289.3270	91.0770	223.9000	628.3000	1.748	62.0000	1.292	36.1000

	8		0	0				
31	318.712	84.670	213.5000	615.8000	1.723	69.1000	1.492	33.5560
32	273.7144	78.120	201.7000	560.4000	1.701	59.5000	1.3556	30.9700
33	239.2699	73.230	189.8000	524.5000	1.698	58.3000	1.260	29.0300
34	233.2633	65.530	187.1000	509.2000	1.617	54.8000	1.246	25.9700
35	191.2266	57.040	166.2000	435.5000	1.602	47.1000	1.150	22.6100
36	267.3222	82.880	222.3000	599.8000	1.668	52.9000	1.202	32.8500

Table A-III Regression parameters and quality of correlation when physicochemical parameters are used ($pMIC_{ab}$)

Model No.	**Parameter used**	**A_i=(1-6)**	**B**	**Se**	**R^2**	**R^2_A**	**F**
1	MW	0.0032(±0.0005)	0.48557	0.08100	0.55445	0.54144	42.31200
2	MR	0.0109(±0.0017)	0.50411	0.08400	0.52000	0.50059	36.83300
3	POL	0.0275(±0.0045)	0.50433	0.08411	0.51999	0.50058	36.82300
4	PC	0.0014(±0.0003)	0.51113	0.09303	0.40303	0.38585	22.96

			8	7	2	6	90
5	IR	1.4491(±0.3444)	-1.06599	0.09844	0.34244	0.32300	17.70000
6	ST	0.0099(±0.0025)	0.77599	0.09999	0.32133	0.30144	16.09700
7	D	0.6835(±0.1896)	0.46433	0.10332	0.27666	0.25533	13.00010
8	MV	0.0028(±0.0009)	0.74022	0.10800	0.20069	0.18350	8.868000
9	MRD	0.0092(±0.0018) 0.3638(±0.1593)	0.17433	0.07933	0.58555	0.56044	23.31100
10	DPOL	0.3638(±0.1593) 0.0231(±0.00	0.17455	0.07933	0.58555	0.56033	23.30400

		46)					
11	MWIR	0.0027(±0.0006) 0.4923(±0.3574)	-0.18755	0.07999	0.57887	0.55531	22.66300
12	MRST	0.0088(±0.0019) 0.0048(±0.0023)	0.39488	0.08022	0.57622	0.55055	22.43100
13	STPOL	0.00477(±0.0023) 0.0222(±0.0049)	0.39499	0.08022	0.57611	0.55044	22.42400
14	MVPC	-0.0074(±0.0020) 0.0039(±0.0007)	0.61288	0.08055	0.57211	0.54611	22.05700
15	PCD	0.0013(±0.0003) 0.5417(±0.1513)	-0.06662	0.08077	0.57022	0.54411	21.88900
16	MW	0.0028(±	0.	0.	0.	0.	21

	ST	0.0006) 0.0028(±0.0026)	4447	0808	5697	5436	.84840
17	MRMV	0.0155(±0.0029) - 0.0023(±0.0012)	0.6417	0.0809	0.5687	0.5426	21.75770
18	MVPOL	- 0.0023(±0.0012) 0.0391(±0.0074)	0.6418	0.0809	0.5686	0.5424	21.74500
19	MRDPOL	1.5411(±2.2556) 0.3705(±0.1609) - 3.8647(±5.6900)	0.1586	0.0799	0.5914	0.5531	15.4441
20	MWMRMV	0.0019(±0.0015) 0.0085(±0.00	0.5932	0.0803	0.5876	0.5489	15.1999

		64) - 0.0019(± 0.0013)					
21	MWMVPOL	0.0019(± 0.0015) - 0.0019(± 0.0013) 0.0215(± 0.0162)	0.5932	0.0803	0.5875	0.5489	15.1955
22	MRIRD	0.0094(± 0.0022) - 0.1730(± 0.7029) 0.4348(± 0.3306)	0.3500	0.0804	0.5863	0.5475	15.1188
23	IRDPOL	- 0.1733(± 0.7031) 0.4349(± 0.3306) 0.0238(± 0.00	0.3504	0.0804	0.5863	0.5475	15.1144

		55)					
24	MVPCST	-0.0249(±0.0169) 0.0107(±0.0065) -0.0179(±0.0171)	1.4505	0.0804	0.5862	0.5474	15.1110
25	MWMRD	0.0002(±0.0021) 0.0085(±0.0065) 0.3449(±0.2348)	0.1885	0.0805	0.5857	0.5469	15.0800
26	MWDPOL	0.0002(±0.0021) 0.3444(±0.2347) 0.0213(±0.0164)	0.1889	0.0805	0.5856	0.5468	15.0760
27	MRPCD	0.0086(±0.0078) 8.77	0.156	0.080	0.585	0.546	15.07

		32(± 0.0011) 0.3751(± 0.2146)	4	5	6	8	50
28	MRSTD	0.0092(± 0.0020) -0.0004(± 0.0065) 0.3900(± 0.4573)	0.1597	0.0805	0.5856	0.5467	15.0730
29	MRMVIRD	0.0355(± 0.0277) -0.0088(± 0.0093) -2.6994(± 2.7679) 0.4522(± 0.3316)	4.3574	0.0806	0.5979	0.5460	11.5230
30	MVIRDP	-0.0088(± 0.0094) -	4.3319	0.0806	0.5976	0.5457	11.5111

	O L	2.68 37(± 2.77 16) 0.45 27(± 0.33 18) 0.08 92(± 0.07 004)					0
3 1	M W M R I R D	- 0.01 37(± 0.01 49) 0.05 64(± 0.05 12) - 4.63 23(± 4.90 57) 3.35 43(± 3.19 56)	4 . 0 6 0 6	0 . 0 8 0 6	0 . 5 9 7 3	0 . 5 4 5 3	1 1 . 4 9 4 0
3 2	M W I R D P O L	- 0.01 33(± 0.01 49) - 4.52 29(± 4.88 99) 3.28 18(± 3.18 44)	3 . 9 7 0 6	0 . 0 8 0 7	0 . 5 9 6 8	0 . 5 4 4 7	1 1 . 4 7 0 0

		0.13 93(± 0.12 86)					
33	MWMRIRPOL	0.00 17(± 0.00 16) 1.46 63(± 2.34 44) 0.54 39(± 0.37 09) -3.69 06(± 5.91 27)	-0.2812	0.0815	0.5881	0.5350	11.0670
34	MWMVIRPOL	0.00 20(± 0.00 16) -0.00 94(± 0.00 94) -2.17 46(± 2.69 99) 0.07 64(± 0.07 01)	4.0495	0.0807	0.5960	0.5439	11.4330
35	MRMVI	0.04 13(± 0.02 87) -	5.693	0.081	0.593	0.540	11.29

	RST	0.0109(±0.0097) -3.3892(±3.0312) 0.0068(±0.0056)	9	0	1	6	80
36	MWMRMVPOL	0.0017(±0.0016) 1.4844(±2.3276) -0.0020(±0.0013) -3.7212(±5.8687)	0.5936	0.0811	0.5929	0.5404	11.28660
37	MRPCIRST	0.0661(±0.0509) -0.0074(±0.0066) -5.4968(±4.88	8.2129	0.0811	0.5929	0.5403	11.28660

		89) 0.02 467(±0.0 181)						
38	MVIRSTPOL	-0.0109(±0.0097) -3.3726(±3.0362) 0.0068(±0.0056) 0.1038(±0.0725)	5.6675	0.0811	0.5929	0.5403	11.2850	

A-IV Actual and predicted value

S.No.	**Actual value (pMIC$_{ab}$)**	**Predicted value (pMIC$_{ab}$)**	**Residual**

	C a b)		
1	1 . 0 8 0	1. 26 3	- 0 . 1 8 3 0
2	1 . 4 0 0	1. 24 6	0 . 1 5 4
3	1 . 3 5 0	1. 40 9	- 0 . 0 5 9
4	1 . 2 3 0	1. 35 1	- 0 . 1 2 1
5	1 . 5 3 0	1. 34 7	0 . 1 8 3
6	1 . 6 1 0	1. 50 4	0 . 1 0 6
7	1 . 4 3 0	1. 37 0	0 . 0 5 9
8	1 .	1. 28	0 .

	4.000	4	1.116
9	1.360	1.403	-0.0430
10	1.220	1.148	0.072
11	1.310	1.316	-0.0006
12	1.390	1.472	-0.082
13	1.360	1.403	-0.043
14	1.280	1.458	-0.178
15	1.310	1.316	-0.0006

16	1.240	1.458	-0.0690
17	1.670	1.456	0.2144
18	1.190	1.242	-0.5222
19	1.150	1.177	-0.0270
20	1.380	1.339	0.0411
21	1.120	1.147	-0.0266
22	2.110	1.309	-0.0990
23	1.19	1.114	0.07

	0		6
24	1.150	1.079	0.071
25	1.360	1.391	-0.031
26	1.170	1.206	-0.036
27	1.260	1.403	-0.144
28	1.440	1.374	0.066
29	1.600	1.570	0.029
30	1.460	1.482	-0.022
31	1.51	1.504	0.00

	0		6
3	1	1.	0
2	.	37	.
	5	4	1
	4		6
	0		6
3	1	1.	0
3	.	27	.
	3	0	1
	8		1
	0		0
3	1	1.	-
4	.	23	0
	1	2	.
	7		0
	0		6
			2
3	0	1.	-
5	.	12	0
	9		.
	8		1
	0		3
			2
3	1	1.	-
6	.	38	0
	3	0	.
	3		0
	0		5
			0

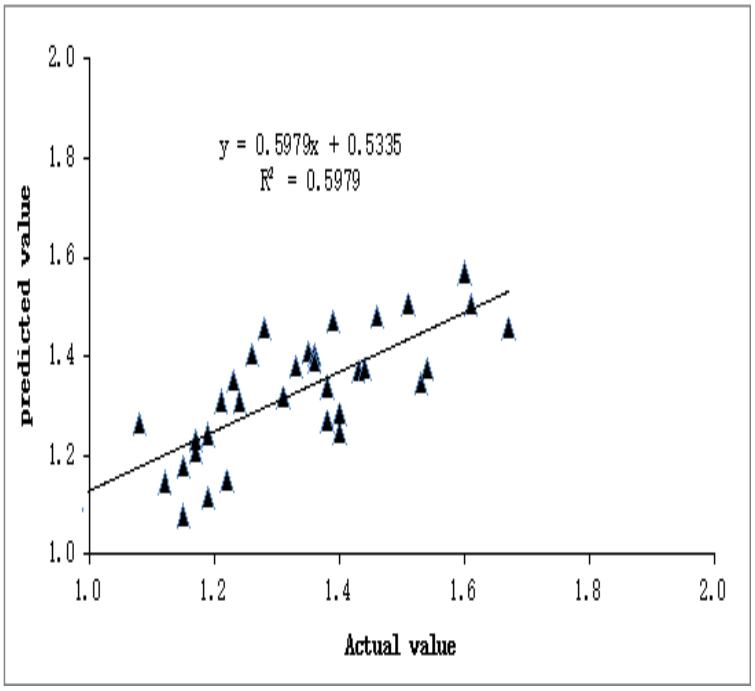


Fig. (a) correlation between actual and predicted $pMIC_{ab}$ values.

Table A-V Cross- validated parameters for the best obtained models

Model No.	**Parameters used**	**PRESS/SSY**	**R^2_{cv}**	**Sprress**	**PSE**
1	MW	0.8036	0.1964	0.0184	0.0174
9	MRD	0.7078	0.2922	0.0183	0.0168
19	MRDPOL	0.6908	0.3092	0.0187	0.0167
30	MVIRDPOL	0.6733	0.3267	0.0192	0.0165

B} Modeling $pMIC_{am}$ using physicochemical parameter

A close look of tableB-I revels that

1) Out of Eight mono-parametric model,MW shows the highest regression value for the best model.

2) Out of ten bi-parametric model,PC and D together shows the highest regression value for the best model.
3) Out of ten tri-parametric model,MW,MR and POL together shows the highest regression value for the best model.
4) Out of ten tetra-parametric model,MR, PC , D and POL together shows the highest regression value for the best model.

Mono-Parametric model

$pMIC_{am}$ = 0.0027(±0.0004)MW + 0.5936 (B-1)
N=37,R^2=0.5511,R^2A=0.5379,Se=0.0696, F=41.7360
When PC and D were taken together a bi-Parametric model has been obtained with improved statistics here R^2 comes out to be 0.5581.

Bi-Parametric model

$pMIC_{am}$ = 0.0011(±0.0002)PC + 0.4063 (±0.1281)D +0.1628
(B-2)
N=37, R^2 = 0.5581, R^2A = 0.5313,Se=0. 0701, F=20.8410
A tri-Parametric model has been obtained when MW,MR and POL were taken together. In this model the R^2 shows significant improvement.

Tri-Parametric model
$pMIC_{am}$ = 0.0028(±0.0013)MW+1.9426(±1.9498)MR
-4.9013(±4.9174)POL + 0.5864 (B-3)
N=37,R^2 =0.5649,R^2A=0.5242,Se=0.0706,F=13.8510
A tetra-parametric model has been obtained when MR, PC, D and POL were taken together. In this model the R^2 shows significant improvement.

Tetra-Parametric model

However,very small improvement is observed in a tetra-parametric model when MR,PC,D and POL have been taken as correlating parameter. This model has been found to be excellent for modeling activity of the compounds of the present study.
$pMIC_{am}$=2.2019(±1.9775)MR+0.0011(±0.0009)PC+0.4257(±0.1846)D+5.5558(±4.9858)POL+
0.1328 (B-4) N=37,R^2=0.5759,R^2A=0.5212,Se=0.0709, F =10.5250.

Validation of model

The model has been validated by plotting a graph actual and predicted value of $pMIC_{am}$ activity as recorded in Table B-II obtained from tetra- parametric model.

Cross- validated parameters

In this we observed the parameter with the high regression value which will obtained the best result.

We have estimated $pMIC_{am}$ values using Model-29. The predictive power of best Model has been obtained by plotting graph between actual and predicted $pMIC_{am}$ values demonstrated in Fig. (b).

This clearly indicates that this is best model for estimating predicting $pMIC_{am}$ values of the compounds in the present study.

Table B-I Regression parameters and quality of correlation when physicochemical parameters are used ($pMIC_{am}$)

Model No.	**parameter used**	**A_i =(1-6)**	**B**	**Se**	**R^2**	**R^2_A**	**F**
1	MW	0.0027(±0.0004)	0.5936	0.0696	0.5511	0.5379	41.73600
2	MR	0.0087(±0.0016)	0.6332	0.0749	0.4809	0.4656	31.49500
3	POL	0.0220(±0.0039)	0.6	0.0	0.4	0.4	31.

			3 3 3	7 4 9	8 0 7	6 5 5	4 7 6 0
4	P C	0.001 2(±0. 0002)	0 . 5 9 6 3	0 . 0 7 8 9	0 . 4 2 3 5	0 . 4 0 6 5	2 4 . 9 7 6 0
5	S T	0.007 7(±0. 0021)	0 . 8 6 3 6	0 . 0 8 8 1	0 . 2 8 1 1	0 . 2 6 0 0	1 3 . 2 9 7 0
6	I R	1.033 5±(0. 3073)	- 0 . 4 1 2 5	0 . 0 9 0 0	0 . 2 4 9 6	0 . 2 2 7 5	1 1 . 3 0 8 0
7	M V	0.002 5(±0. 0007)	0 . 7 6 7 7	0 . 0 9 0 7	0 . 2 3 8 7	0 . 2 1 6 3	1 0 . 6 5 8 0
8	D	0.529 9(±0. 1625)	0 . 6 2 5 3	0 . 0 9 0 7	0 . 2 3 8 3	0 . 2 1 5 9	1 0 . 6 3 6 0
9	P C D	0.001 1(±0. 0002) 0.406 3(±0. 1281)	0 . 1 6 2 8	0 . 0 7 0 1	0 . 5 5 8 1	0 . 5 3 1 3	2 0 . 8 4 1 0
1 0	M W S T	0.002 4(±0. 0005) 0.001	0 . 5 7	0 . 0 7	0 . 5 5	0 . 2 3	2 0 . 7

		5(±0.0022)	19	02	72	03	61
11	MWMV	0.0029(±0.0006) -0.0004(±0.0008)	0.624	0.0704	0.5539	0.5268	20.4850
12	MWD	0.0025(±0.0003) 0.0694(±0.1582)	0.5424	0.0705	0.5537	0.5266	20.4690
13	MWIR	0.0025(±0.0005) 0.1273(±0.3074)	0.4195	0.0705	0.5534	0.5263	20.4450
14	MWPC	0.0029(±0.0009) -0.0001(±0.0005)	0.6094	0.0706	0.5520	0.5249	20.3330
15	MWPOL	0.0029(±0.0013) -0.0018(±0.0111)	0.5972	0.0706	0.5514	0.5243	20.2850
16	MWMR	0.0029(±0.0013) -0.007(±0.0044)	0.5972	0.0706	0.5514	0.5242	20.2840
17	MVD	0.0029(±0.0006) 0.6119(±0.1278)	-0.085	0.0707	0.5507	0.5235	20.2260

			8				0
18	MVPC	-0.0054(±0.0018) 0.0031(±0.0006)	0.6694	0.0707	0.5503	0.5231	20.19200
19	MWMRPOL	0.0028(±0.0013) 1.9426(±1.9498) -4.9013(±4.9174)	0.5864	0.0706	0.5649	0.5242	13.85100
20	MWMVPC	0.0016(±0.0019) -0.0028(±0.0035) 0.0014(±0.0020)	0.6412	0.0710	0.5606	0.5194	13.60800
21	MWSTD	0.0025(±0.0005) 0.0034(±0.0053) -0.1561(±0.3827)	0.6583	0.0711	0.5595	0.5182	13.54600
22	MWPCST	0.0018(±0.0018) 0.0003(±0.0008) 0.0025(±0.0034)	0.5214	0.0711	0.5592	0.5179	13.53100
23	MWI	0.0025(±0.0006)	0.8	0.0	0.5	0.5	13.

	RST	-0.2511(±0.6624) 0.0030(±0.0047)	919	711	592	178	52900
24	PCDPOL	0.0013(±0.0009) 0.4387(±0.1849) -0.0042(±0.0170)	0.119	0.0711	0.5590	0.5176	13.51900
25	PCIRD	0.0011(±0.0002) -0.1348(±0.5492) 0.4669(±0.2791)	0.29888	0.0711	0.5590	0.5176	13.51800
26	MRPCD	-0.0016(±0.0068) 0.0013(±0.0009) 0.4382(±0.1849)	0.12002	0.0711	0.5589	0.5176	13.51700
27	MVPCD	-0.0012(±0.0055) 0.0016(±0.0020) 0.0318(±0.4036)	0.27433	0.0711	0.5589	0.5175	13.51300
28	MWM	0.0019(±0.0018)	0.4	0.0	0.5	0.5	13.

	V S T	0.0006(±0.0019) 0.0029(±0.0049)	9 9 2	7 1 1	5 8 7	1 7 3	5 0 4 0
29	M R P C D P O L	2.2019(±1.9775) 0.0011(±0.0009) 0.4257(±0.1846) -5.5558(±4.9858)	0 . 1 3 2 8	0 . 0 7 0 9	0 . 5 7 5 9	0 . 5 2 1 2	1 0 . 5 2 5
30	M W M R S T P O L	0.0020(±0.0015) 2.2033(±1.9854) 0.0019(±0.0024) -5.5550(±5.0065)	0 . 5 4 8 6	0 . 0 7 1 0	0 . 5 7 4 2	0 . 5 1 9 2	1 0 . 4 5 1 0
31	M R I R D P O L	2.2203(±1.9907) -0.6538(±0.6166) 0.5473(±0.2876) -5.5797(±5.0221)	1 . 0 2 9 9	0 . 0 7 1 2	0 . 5 7 1 9	0 . 5 1 6 7	1 0 . 3 5 5 0
32	M R M V	2.2751(±1.9874) -	0 . 6 6	0 . 0 7	0 . 5 7	0 . 5 1	1 0 . 3

	PCPOL	0.006(±0.0028) 0.0036(±0.0019) -5.7439(±5.0109)	22	13	10	56	140
33	MWMRDPOL	0.0019(±0.0019) 2.1811(±2.0057) 0.1285(±0.2067) -5.4972(±5.0569)	0.4792	0.0713	0.5703	0.5149	10.2860
34	MWMRMVPOL	0.0025(±0.0013) 2.1505(±1.9978) -0.0007(±0.0011) -5.4202(±5.0371)	0.6281	0.0713	0.5702	0.5147	10.2810
35	MRMVDPOL	2.2779(±1.9902) 0.0020(±0.0021) 0.5155(±0.2770) -5.7404(±5.0185)	0.0312	0.0714	0.5698	0.5143	10.2650

36	MWMRIRPOL	0.0025(±0.0014) 2.1501(±2.0018) 0.1853(±0.3167) -5.4242(±5.0485)	0.331	0.071	0.569	0.514	10.2600
37	MRIRSTPOL	2.2893(±1.9972) -0.7960(±0.7112) 0.00853(±0.0047) -5.7552(±5.0386)	1.5275	0.071	0.567	0.511	10.7180
38.	MWMRPCPOL	0.0027(±0.0013) 2.0679(±2.0042) -0.0003(±0.0007) -5.2129(±5.0527)	0.609	0.071	0.569	0.511	10.1450

Table B-II Actual and predicted value

S. No.	**Actual value ($pMIC_{am}$)**	**Predicted value ($pMIC_{am}$)**	**Residual**
1	1.160	1.214	-0.054
2	1.360	1.262	0.098
3	1.350	1.357	-0.007
4	1.270	1.295	-0.025
5	1	1.	0

	.3900	325	.0650
6	1.530	1.459	.0710
7	1.330	1.339	-0.0090
8	1.360	1.276	.0840
9	1.420	1.371	.0490
10	1.160	1.137	.0230
11	1.310	1.306	.0040
12	1.330	1.393	-0.063
13	1.300	1.371	-0.071
11	1	1.	-

4	.320	421	0.1010
15	1.250	1.292	-0.042
16	1.220	1.296	-0.076
17	1.730	1.378	0.352
18	1.170	1.234	-0.064
19	1.130	1.166	-0.036
20	1.440	1.412	0.028
21	1.100	1.156	-0.056
22	1.	1.233	-0.

	9 0		0 4 3
2 3	1 . 1 9 0	1. 13 1	0 . 0 5 9
2 4	1 . 1 5 0	1. 07 2	0 . 0 7 8
2 5	1 . 3 0 0	1. 35 1	- 0 . 0 5 1
2 6	1 . 2 1 0	1. 19 5	0 . 0 1 5
2 7	1 . 3 0 0	1. 37 1	- 0 . 0 7 1
2 8	1 . 3 4 0	1. 30 4	0 . 0 3 6
2 9	1 . 4 6 0	1. 41 7	0 . 0 4 3
3 0	1 . 2 4 0	1. 36 9	- 0 . 1 2 9
3 1	1 .	1. 45	- 0

	4 1 0	9	. 0 4 9
3 2	1 . 4 0 0	1. 30 4	0 . 0 9 6
3 3	1 . 2 8 0	1. 23 3	0 . 0 4 7
3 4	1 . 1 5 0	1. 25 6	- 0 . 1 0 6
3 5	1 . 0 6 0	1. 10 3	- 0 . 0 4 3
3 6	1 . 2 7 0	1. 32 0	- 0 . 0 5 0

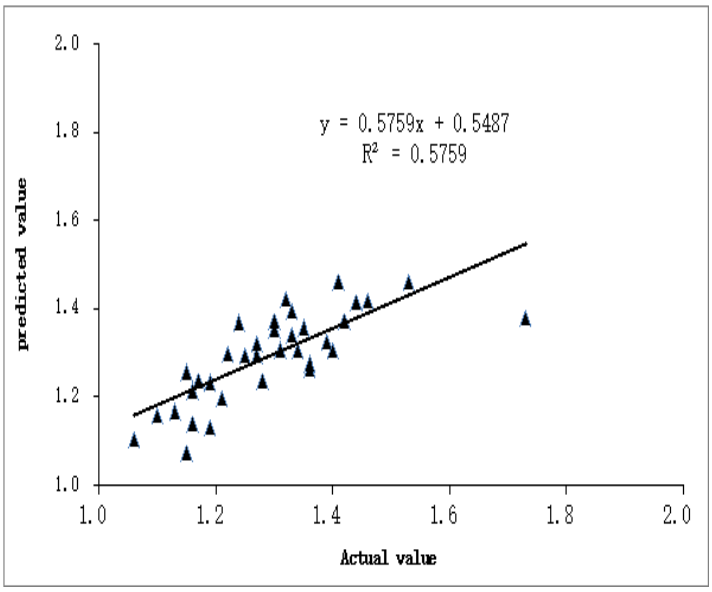


Fig. (b) correlation between actual and predicted $pMIC_{am}$ values.

Table B-III Cross- validated parameters for the best obtained models

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Model No.	**Parameters used**	**PRESS/SSY**	**R^2_{cv}**	**Spress**	**PSE**
1	MW	0.81466	0.18544	0.01544	0.01466
9	PCD	0.79177	0.20833	0.01558	0.01455
19	MWMRPOL	0.77701	0.22999	0.01662	0.01444
30	MWMRSTPOL	0.07422	0.92588	0.01665	0.01422

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