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Research Article

Modlling of Inhibitory Activities of Sulphanilamide Schiff Bases Using Physicho Chemical Parametors With Log Ca Ii Activities

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Abstract

Inhibitory activities of a series of sulphonilamide Schiff bases have been modeled using physic chemical parameters with log CAII activity .the results show that they are best modeled in multi parametric modeling.

Key Words:Inhibitory activity modeling sulphanilamides Schiff bases With log CAII.

Introduction

Quantitative structure-property-activity relationship (QSPR and QSAR) have been established as a well known research tool and are being widely used in the field of pharmaceutical chemistry. Industry and environmental studies [1-4], the basic assumption. Underlying in QSPR/QSAR studies is that the 2, 3 structure of a molecule determines it's behavior.

Agrawal and co-workers have reported[5-9] modeling of log (IC_{50}) CA-II inhibitors using topological indices. Now we are trying to use the physicochemical parameters for modeling of inhibitory activities of sulphonilamide. Schiff bases reported by Saxena and Khadikar [10] who have used the wiener index to model the inhibitory activities of the Schiff bases. They have splitted 35 computers into several groups and proposed excellent models. Sueha splitting was due to adoption of simple rogation analysis. The study was carried out on the compound prepared by supuran et. al.[11, 12] (Table 1). They have used activities of sulphonilamide Schiff bases against CA-II isozymes. Saxena and Khadikar[13] have successfully modeled these activities using the wiener index[14].

Parameters Used:-

We have used chamsketch program of ACD lab for calculation various physicochemical parameters, viz, molecular weight (MW), molar refraction (MR), Molar volume (MV), parachor (PR) surface tension (γ), density (d), polarisability (α), and index of refraction (n) and adopted step-wise regression analysis obtaining a model with best statistics, the calculated parameters for all the 35 compounds are reported in Table 2.

Correlation Matrix:-

We have studding the inter-correlation of all the parameters. Along with the one biological activities. And three indicator parameters such a correlation matrix is reported in table 3.parameters showing good correlation with lg Ic_{50} (CAII),MW, MR, MV, PR and α are the parameters which show good correlation with Ic_{50} (NM) Log Ic_{50} (CA-II) inhibitory activity.

Results and Discussion

Sulphanilamide Schiff bases used in the present study are reported in Table1. Table 1 also shows the log (CAII) activity of the compounds. We have also used three indicators parameters viz, IP, IP_2 and IP_3 to understand the effect of various substituent's at R_Z position .the labials of the indicator parameters and their values are described in Table 1. Various physicochemical parameters calculated using ACD LAB software is reported in Table 2. Table 3 shows the correlation of these parameters as well as their correlation with LOG (CA-II). On the basis of correlation matrix,

We may in for that MR, MV, γ, α, and IP_2 modeling the LOG (CA-II) activity. Six parametric models is,

$$= -0.0789(\pm 0.0235)MR + 0.0159(\pm 0.0062)MV + 0.0835(\pm 0.0306)\gamma$$
$$- 6.0123(\pm 1.9412)d + 0.0427(\pm 0.0339)$$
$$\propto -1.4256(\pm 0.1864)IP_2 + 5.2955$$

$$n = 31,\ ss = 0.2834,\ R = 0.9077,\ F = 18.719,\ Q = 3.2028$$

Calculation :-

We have calculated LOG CA II activity values using the best six parametric models as discussed above. The values so calculated are reported in Table - 4 comparisons between observed and estimated LOG CA II values are shown in figure 2. The predictive R^2 value comes out to be 0.8240.

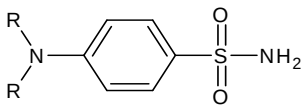

Figure 1

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Table 1. Compounds used in the present study, their LOG (CA II) and Indicator values.

Comp. No.	R1	R2	Log(CA II)	IP1	IP2	IP3
1.	Phenyl	H	1.4313	1	0	0
2.	2-hydroxy phenyl	H	1.6127	1	0	0
3.	2-nitrophenyl	H	1.3222	1	0	0
4.	4-chlorophenyl	H	1.4471	1	0	0
5.	4-hydroxy phenyl	H	1.2787	1	0	0
6.	4-methoxy phenyl	H	0.9030	1	0	0
7.	4-dimethyl amino phenyl	H	0.6989	1	0	0
8.	4-nitro phenyl	H	1.0413	1	0	0
9.	4-cinophenyl	H	0.9030	1	0	0
10.	3-methoxy-4-hydroxy phenyl	H	0.4771	1	0	0
11.	3,4-dimethoxy phenyl	H	1.0000	1	0	0
12.	3-methoxy-4-acetoxy phenyl	H	0.3010	1	0	0
13.	2,3-dihydroxy-5-formyl phenyl	H	0.4771	1	0	0
14.	2-hydroxy-3-methoxy 5-formyl phenyl	H	0.4771	1	0	0
15.	3,4,5-trimethoxy phenyl	H	0.4771	1	0	0
16.	3-methoxy-4-hydroxy formyl phenyl	H	0.6020	1	0	0
17.	2-furyl	H	0.6189	1	0	0
18.	3-methoxy-2-furyl	H	0.6020	1	0	0
19.	Pyrole-2-yl	H	0.3010	1	0	0
20.	Imidazole-4(5)-yl	H	1.0791	1	0	0
21.	2-pyridyl	H	0.9542	1	0	0
22.	3-pyridal	H	0.9030	1	0	0
23.	4-pyridal	H	0.6189	1	0	0
24.	styryl	methyl	-0.4089	0	1	0
25.	4-methoxy styryl	methyl	-0.9208	0	1	0

Comp. No.	R1	R2	Log(CA II)	IP1	IP2	IP3
26.	4-dimethylamino stryl	methyl	-1.0000	0	1	0
27.	3,4,5-trimethoxy styryl	methyl	-0.6197	0	1	0
28.	styryl	phenyl	-0.2518	0	0	1
29.	4-methoxy styryl	phenyl	0.7403	0	0	1
30.	4-dimethyl amino styryl	phenyl	0.2278	0	0	1
31.	3,4,5-trimrthoxy styeyl	phenyl	0.3710	0	0	1
32.	3,4,5-trimethoxy styryl	4-methoxy phenyl	0.1038	0	0	0
33.	3-nitroso styryl	4-methoxy methyl	-0.1870	0	0	0
34.	3,4,5-trimethoxy styryl	4-amino phenyl	-0.0705	0	0	0
35.	3,4,5-trimethoxy styryl	4-phenyl phenyl	0.3944	0	0	0

Table 2. Values of physicochemical parameters calculated for compounds :-

No.	MW	MR	MV	Pr	n	γ	d	α
1.	260.313	72.08	206.6	554.7	1.614	51.8	1.25	28.57
2.	276.312	72.93	203.6	56.4	1.633	56.9	1.35	28.81
3.	305.310	77.74	212.0	600.1	1.654	64.1	1.43	30.18
4.	294.757	76.68	216.0	583.5	1.628	53.2	1.36	30.39
5.	276.312	72.93	203.9	56.4	1.633	56.9	1.35	38.91
6.	390.339	77.89	228.1	604.9	1.597	49.2	1.27	30.87
7.	303.381	84.88	247.9	651.0	1.600	47.5	1.22	33.65
8.	305.310	77.74	212.0	6001.0	1.654	64.1	1.43	30.81
9.	285.322	78.60	219.5	6005.0	1.634	55.9	1.29	31.16
10.	306.338	78.74	225.6	610.6	1.614	53.6	1.35	31.21
11.	320.365	83.70	250.1	655.2	1.584	47.1	1.28	33.18
12.	348.376	89.16	263.4	699.5	1.592	49.7	1.32	35.34
13.	320.332	79.24	214.6	610.3	1.66	65.4	1.49	31.41
14.	334.348	84.20	239.0	654.9	1.622	56.3	1.39	33.38
15.	350.391	89.51	271.7	705.5	1.572	45.4	1.28	35.48
16.	385.234	86.30	338.2	854.2	1.644	56.8	1.61	34.21
17.	250.275	64.25	180.9	496.6	1.628	56.7	1.38	25.47
18.	264.301	68.67	196.2	527.7	1.617	52.3	1.34	27.22
19.	249.290	65.91	179.2	497.2	1.656	59.2	1.39	26.13
20.	250.278	64.36	167.8	478.4	1.692	66.0	1.49	25.91

21.	261.301	70.52	195.3	535.8	1.641	56.6	1.33	27.95
No.	**MW**	**MR**	**MV**	**Pr**	**n**	**γ**	**d**	**α**
22.	261.301	70.52	195.3	535.8	1.641	56.6	1.33	27.95
23.	261.301	-----	-----	-----	-------	-----	------	-----
24.	300.377	85.53	253.2	655.5	1.590	44.9	1.18	33.90
25.	330.402	91,35	274.9	705.7	1.578	43.4	1.2	36.21
26.	343.444	98.34	294.4	751.8	1.582	42.5	1.16	38.98
27.	390.454	102.97	318.2	806.3	1.560	41.2	1.22	40.82
28.	362.446	106.21	305.9	801.3	1.611	47.0	1.18	42.19
29.	392.472	112.03	327.5	851.5	1.599	45.6	1.19	44.41
30.	405.514	119.02	347.0	897.6	1.601	44.7	1.16	47.18
31.	452.524	123.65	370.8	952.0	1.581	43.4	1.22	49.02
32.	482.550	129.47	392.4	1002.3	1.573	42.5	1.22	51.32
33.	437.470	117.69	332.8	897.0	1.625	52.7	1.31	46.65
34.	367.509	125.57	367.5	959.2	1.598	46.3	1.27	49.78
35.	528.620	148.76	438.5	1128.9	1.593	43.9	1.20	68.97

MW - Moleculer Weight, MR - Molar Refraction, MV - Molar Valume
Pr - Parachor, γ - Purface Tension, d - Density,
A - Polarization n - Index of Refraction.

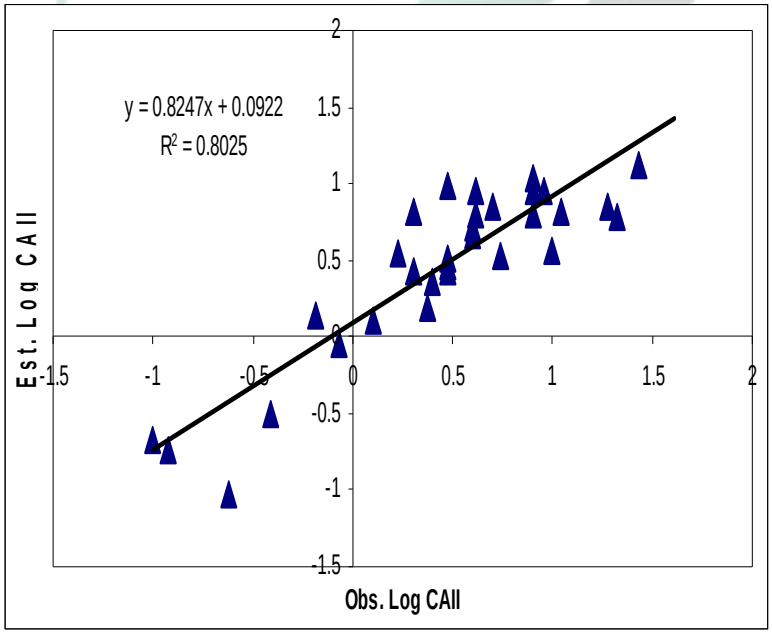

Figure 2. : Comparison of observed and estimated logCAII using model-31

Table 3. Correlation matrix for the intercorrelaton of structural descriptors and their correlation with LOG CA II activity

	Lg (CA II)	MW	MR	MV	Pr	n	γ	d	α	IP_1	IP_2	IP_3
LgCA II	1.0000											
MW	-0.4131	1.0000										
MR	-O.4941	0.9234	1.0000									
MV	-05118	0.9355	0.9609	1.0000								
Pr	0..815	0.0072	0.0173	-0.0094	1.0000							
n	0.5540	-0.5717	-0.5933	0.6237	0.1459	1.0000						
γ	0.6032	-0.6086	-0.6803	-0.7061	0.1815	0.9511	1.0000					
d	0.4863	-0.4016	-0.5586	-0.4799	0.0569	0.7817	0.8555	1.0000				
α	-0.4530	0.9182	0.9876	0.9540	0.0202	-0.5593	-0.6502	-0.5369	1.0000			
IP_1	0.7373	-0.6944	0.8342	-0.7984	0.0984	0.5944	0.7240	0.6930	-0.7942	1.0000		
IP_2	-0.7081	0.0425	0.0934	0.1343	-0.0683	-0.4570	-04542	-0.4116	-0.0737	-0.4973	1.0000	
IP_3	-0.1359	0.3648	0.4463	0.4104	-0.0267	-0.2104	-0.3430	-0.4203	0.3910	-0.4973	-0.1290	1.0000

Table 4- comparison of estimated biological activity (LOG CA II) with Their observed values using model -31.

Comp. No.	Observed log CAII	Estimated CAII log	
		Model-31	Residue
1.	1.4313	1.1280	0.3033
2.	1.6127	------	-------
3.	1.3222	0.7860	0.5362
4.	1.4471	------	-------
5.	1.2787	0.8540	0.4247
6.	0.9030	0.7930	0.1100
7.	0.6989	0.8540	-0.1551
8.	1.0413	0.8130	0.2283
9.	0.9030	1.0440	-0.1410
10.	0.4771	0.9850	-0.1079
11.	1.0000	0.5700	0.4300
12.	0.3010	0.4320	-0.1310
13.	0.4771	0.5120	-0.0349
14.	0.4771	0.4580	0.0191
15.	0.4771	0.4320	0.0451
16.	0.6020	0.7220	-0.1200
17.	0.6189	0.8070	-0.1881
18.	0.6020	0.6640	-0.0620
19.	0.3010	0.8240	-0.5230
20.	1.0791	------	-------
21.	0.9542	0.9530	0.0012
22.	0.9030	0.9530	-0.0500
23.	0.6189	0.9530	-0.3341
24.	-0.4089	-0.5000	0.0911
25.	-0.9208	-0.7390	-0.1818
26.	-1.0000	-0.6780	-0.3220
27.	-0.6197	-1.0320	0.4123
28.	-0.2518	-------	-------
29.	0.7403	0.5370	0.2033
30.	0.2278	0.5380	-0.3102
31.	0.3710	0.1840	0.1870
32.	0.1038	0.1130	-0.0092
33.	-0.1870	0.1470	-0.3340
34.	-0.0705	-0.0490	-0.0215
35.	0.3944	0.3600	0.0344

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