International Journal of Science, Environment
and Technology, Vol. 2, No 2, 2013, 230 - 235

MODELING OF (CAII) INHIBITORY ACTIVITY OF SULFONAMIDES

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Abstract: In the present investigation the applicability of various physicochemical parameters are tested for the QSAR / QSPR study on sulfonamides for the modeling of inhibitory activities of sulfonamides. The regression analysis shown that even in the multi parameters correlation of physicochemical parameters give significant regression coefficient further more using combination of physicochemical parameters along with the indicator parameters, a tremendous improvement in the statistics has been observed the results are critically discussed on the basis regression data.
Keywords: QSAR inhibitory (log CAII) activity, modeling sulfonamides.

Introduction

The inhibitory activity of isozymes CAII (Cytosolic form) involves is important physicochemical process for 40 sulfonamides is reported by Supuran et al[1] has carried out an extensive research work in developing quantitative structure activity relationship (QSAR'S) for a large series of carbonic anhydrase & has published several research papers related to this aspect.

Agrawal & Khadikar [2-9] have under taken topological indices to model the CAII inhibitory activity. They have used Wiener index, Szeged index, Balban index, first- order (K), valance connectivity indices & branching index (B), for modeling of biological activity of carbonic anhydrase inhibitors. They gave excellent results [6-9].

Agrawal & Khadikar [2-9] have also published their work in which they have used molecular negontropy to model the CA inhibitory activity of sulfonamides.

Materials & Methods

The study was carried on the compounds prepared by Suparan [7] at al 1996 (Table 1). They have used activities of sulfonamides inhibitory activity (Log (CAII)) the series of sulfonamides used in present study.

Parameters used

We have used chemsketch program of ACD lab for calculation of various physicochemical parameters like molecular weight (MW), molar refraction (MR), molar volume (MV), poacher (PR), Surface Tension (Y), density (D), Polarizarility (α) & index of refraction (N) &

*Received Jan 10, 2013 * Published April 2, 2013 * www.ijset.net*

adopted stepwise regration analysis for obtaining a model with best statistics. The calculated parameters for all 40 compounds are reported in Table 2.

Correlation Matrix

We have studies the inter correlation of the parameters along with the one biological activity & indicator parameters. Such a correlation matrix is reported in table 3 parameters showing very good correlation with log Ki (h CAII), MW, MR, MV, n, IP2, IP3 & IP4 are the parameters with shown good correlation.

Result & Discussion

Sulfonamides used in the present study are reported in table 1. Table 1 also shown the log Ki (h CAII) activity & four indicator parameters IP1, IP2, IP3 & IP4 various physicochemical parameters calculated using ACD lab software are reported in Table 2, Table 3 shown the correlation of these parameters as well as their correlation with log Ki (h CAII) on the basis of correlation matrix, we may infer that MW & IP4 are the parameters which can be used for modeling the log Ki (h CAII) activity. Similarly MV has also got some potential for this purpose. The multi parametric model is-

Log Ki (h CAI) = 0.0018 (±0.0016) MW +0.0132

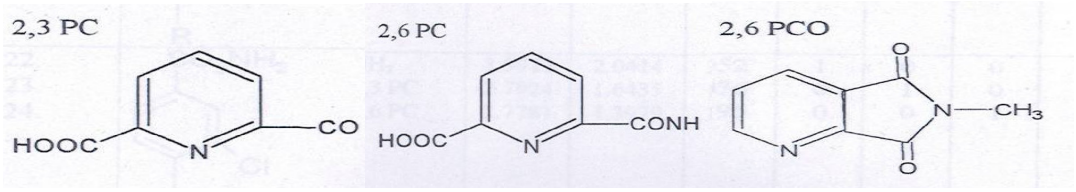
(±0.0079) MR -0.0155 (±0.0038) MV -1.0629 (± 0.0023)

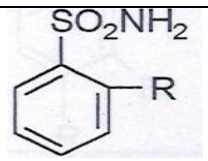
n +0.2785 (±0.1534) IP2 + 0.3877 (±0.1613) IP3 +0.6923 (± 0.1375)

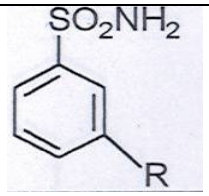
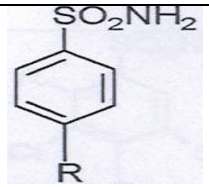
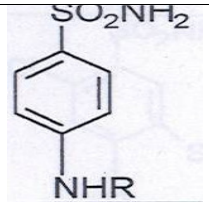
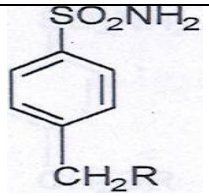
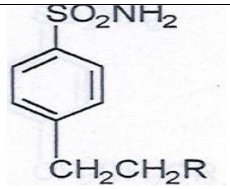
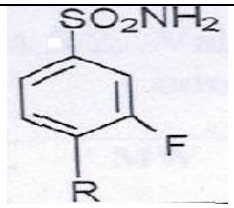
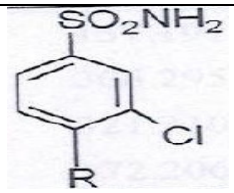
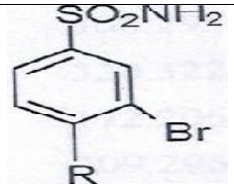
IP4 + 1.7054

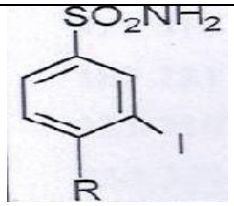
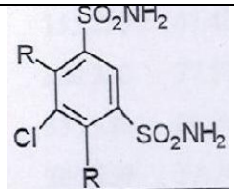
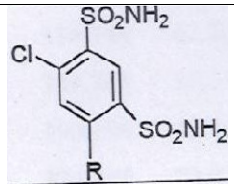
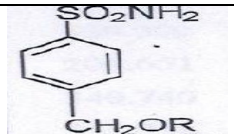
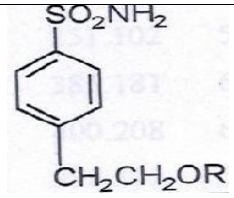
n = 37, SE=0.2859, R=0.8846, F=14.9000, Q=3.0941

Table 1- The structure, inhibition activity logs Ki (hCA I) for a series of sulfonamides used in the present study



Compd. No.	Structure	R	Log Ki(hCAI)	IP1	IP2	IP3	IP4
1.		NH_2	4.6571	1	0	0	0
2.		2,3 PC	4.3222	0	1	0	0
3.		2,6 PC	4.3010	0	0	1	0

4.		NH_2	4.3979	1	0	0	0
5.		2,3 PC	4.3010	0	1	0	0
6.		2,6 PC	4.2672	0	0	1	0
7.		NH_2	4.4472	1	0	0	0
8.		2,3 PC	4.1903	0	1	0	0
9.		2,6 PC	4.1761	0	0	1	0
10.		NH_2	4.8949	1	0	0	0
11.		2,3 PC	4.3324	0	1	0	0
12.		2,6 PC	4.3139	0	0	1	0
13.		NH_2	4.3979	1	0	0	0
14.		2,3 PC	3.0170	0	1	0	0
15.		2,6 PC	2.9345	0	0	1	0
16.		NH_2	4.3222	1	0	0	0
17.		2,3 PC	2.9569	0	1	0	0
18.		2,6 PC	2.7404	0	0	1	0
19.		NH_2	3.9192	1	0	0	1
20.		2,3 PC	2.7324	0	1	0	1
21.		2,6 PC	2.7076	0	0	1	1
22.		NH_2	3.9912	1	0	0	1
23.		2,3 PC	2.7924	0	1	0	1
24.		2,6 PC	2.7781	0	0	1	1
25.		NH_2	3.8129	1	0	0	1
26.		2,3 PC	2.7818	0	1	0	1
27.		2,6 PC	2.7600	0	0	1	1

28.		NH_2	3.7781	1	0	0	1
29.		2,3 PC	2.7853	0	1	0	1
30.		2,6 PC	2.7782	0	0	1	1
31.		NH_2	3.7853	1	0	0	1
32.		2,3 PC	2.6990	0	1	0	1
33.		2,6 PC	2.6532	0	0	1	1
34.		NH_2	3.9243	1	0	0	1
35.		2,3 PC	2.7782	0	1	0	1
36.		2,6 PC	2.5682	0	0	1	1
37.		H	4.3802	0	0	0	0
38.		2,6 PCO	3.3118	0	0	1	0
39.		H	4.2553	0	0	0	0
40.		2,6 PCO	3.3010	0	0	0	0

IP_1 = 1, if NH_2 group is present at R position, otherwise 0

IP_2 = 1, if 2,3 PC group is present at R position, otherwise 0

IP_3 = 1, if 2,6 PC group is present at R position, otherwise 0

IP_4 = 1, if halogen group is present in basic structure, otherwise 0

Table 2: Comparison of estimated biological activity log Ki (h CAII) with their observed values using model–16

Compd.No	**Observed Log Ki (hCAII)**	**Estimated log IC20 (nM) CAII**	
		Model-16	**Residue**
1	2.4698	2.348	0.1218
2	2.4472	2.131	0.3162
3	2.415	2.211	0.204
4	2.3802	2.441	-0.0608

5	2.3979	2.348	0.0499
6	2.3838	2.334	0.0398
7	2.4771	0.334	2.1331
8	2.1206	2.137	-0.0164
9	2.0828	2.211	-0.1282
10	2.5052	2.488	0.0172
11	2.4393	2.447	-0.0077
12	2.4314	2.104	0.3274
13	2.2304	2.17	0.0604
14	1.6232		
15	1.5563		
16	2.2041	2.049	0.1551
17	0.9542	4.591	-0.6368
18	0.8451		
19	1.7782	1.706	0.0722
20	1	1.391	-0.391
21	0.9031	1.472	-0.5689
22	2.0414	1.698	0.3434
23	1.6435	1.383	0.2605
24	1.3979	1.202	0.1959
25	1.6021	1.775	-0.1729
26	1.4917	1.188	0.3037
27	1.4771	1.267	0.2101
28	1.8451	2.068	-0.2229
29	1.5185	1.439	0.0795
30	1.7924	1.652	0.1404
31	2.243	2.362	-0.199
32	1.8388	1.562	0.2798
33	1.7404	1.534	0.2064
34	2.2041	2.329	-0.1249
35	1.7782	1.696	0.0822
36	1.6812	1.682	-0.0008

37	2.7482	2.485	0.2632
38	2.0792	2.369	-0.2898
39	2.6532	2.515	0.1382
40	2.0212	2.398	-0.3768

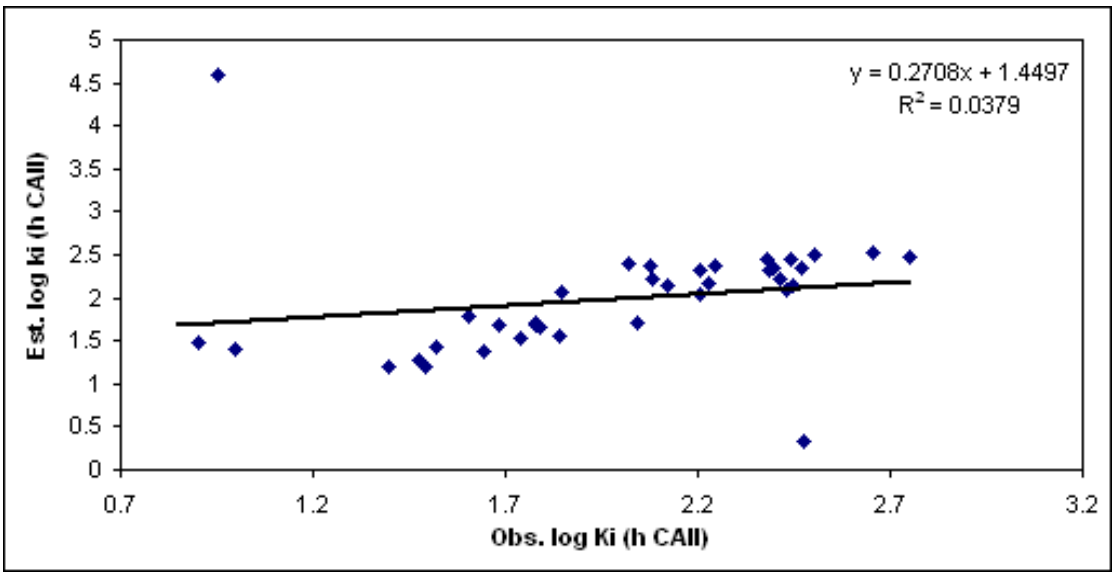


Figure: Comparison of observed & estimated log Ki (h CAII) using model – 9.

Conclusion

On the basis of above rending we conclude that Log Ki (h CAII) activity can be modeled using the physicochemical parameters MW, MR, n, IP2, IP3 & IP4 has been found to be excellent. Our result better then the earlier reported results.

Reference

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