Research Paper Science

QSPR study on benzene disulfonamides with log IC50 (CAII) inhibitory activities.

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ABSTRACT

In the present investigation the applicability of various physicochemical parameters are tested for the QSAR study on sulfonamides for the modeling of benzene disulfonamides. The regration analysis shown that even in the multi parameters correlation of physicochemical parameters give significant regration coefficient further more using combination of physicochemical parameters along with the indicator parameters, a treatment improvement in the statistics has been observed the results are critically discussed on the basis regration data.

Keywords: QSAR study on benzene disulfonamides with log Ic50 (CAII) initiatory activities.

Introduction:-
Aromatic sulfonamides e.g. Sulfonamides have been shown to exhibit inhibitory activity of the zinc enzyme carbonic an hydras because of some clinical abnormality related to the demised CO2 combining power of patients which were related with the newly introduced the rapeutic agent 2 belonging to antibacterial sulfonamides, new potent derivatives were synthesized by the chemistrs they include homosulfonamides 3,4 or the N4 – substituted derivatives 5,6. After this study Krebs pointed out that the aromatic sulfonamides behave as weaker CA inhibitory as compared to the hetrocyclic compounds 7.

Clare & Supuran 8 have prepared foure series of compounds by reaction of sulfonyl halides (Sulfonic acid cyclic an hydrides) with sulfanilamide, metanilamide, p - amino methyl – benzene sulfonamide & p- (2- aminoethyl) - benzene sulfonamide.

The 72 inhibitors were characterized by standard procedures & ascayed for inhibitory of human red cacl isozymes CAII.

In this work we have tried to model Log Ic50 activities of compound as synthesized by Clarke et al 8 using physicochemical parameters.

Materials & Methods:-
The study was carried on the compounds prepared by Clare & Suparan et al 1998 (table 1). They have used activities of sulfonamides inhibitory activity (Log (CAII)) the series of benzene disulfonamides.

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) & adopted stepwise regration analysis for obtaining a model with best statistics. The calculated parameters for all 72 compounds are reported in table 2.

Correlation matrix:-
We have studies the inter correlation of the parameters. Such a correlation matrix is reported in table 3 parameters showing very good correlation with log CAII, MW, MR, n, d, α & IP5 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 (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 with log (CAII) on the basis of correlation matrix, we may infer that MW, MR, n, d & IP5 are the parameters which can be used for modeling the log (CAII) activity the multi parametric is-

Log IC50 (CAI) = -0.0052 (±0.0022) MW -0.0107 (±0.0096) MR +7.8904 (±2.0439) n -2.7393 (±0.7271) d +0.4410 (0.0929) IP5 -4.8888

n = 66, SE=0.2308, R=0.8281, F=26.1830, Q=3.5829

Table: - Comparison of estimated biological activity log IC50 (nM) CAII with their observed values using model – 15.

Compd.No	Observed LogIC50(nM) CAII	Estimated log IC20 (nM) CAII	
		Model-19	Residue
1	1.8062	1.79	0.0872
2	0.2304	1.232	-0.0016
3	1.0792		
4	1.6902	1.622	0.0682
5	1.6232	1.518	0.1052
6	1.7404	1.743	-0.0026
7	0.9542	1.253	-0.2988
8	0.9542	1.202	-0.2478
9	0.9031	0.592	0.3111
10	1.4771	1.277	0.2001
11	0.8451	1.145	-0.2999
12	1.0414	1.114	-0.0726
13	1		
14	1	1.114	-0.114
15	1.9138	1.67	0.7468
16	1.6335	1.594	0.0395
17	1.6627	2.027	-0.3643
18	1.0792	0.733	0.3462
19	1.8976	1.719	0.1786
20	1.4472	1.569	-0.1218
21	1.4913	1.61	-0.1187
22	1.8865	1.7	0.1865
23	1.8808	1.518	0.3628
24	1.8261	1.743	0.0831
25	1	1.23	-0.23
26	0.9542	1.214	-0.2598
27	0.9542	0.592	0.3622
28	1.6021	1.277	0.3251
29	0.8451	1.145	-0.2999
30	1	1.114	-0.114

31	0.9542	1.114	-0.1598
32	1	1.114	-0.114
33	2.0043		
34	1.6721	1.594	0.0781
35	1.6989	1.594	0.1049
36	1.1761	1.166	0.0101
37	1.7076	1.602	0.1056
38	1	1.399	-0.399
39	0.9031	0.884	0.0191
40	1.6021	1.46	0.1421
41	1.4912	1.361	0.1302
42	1.716	1.585	0.131
43	0.8451	1.117	-0.2719
44	0.8451	1.071	-0.2259
45	0.6989	0.485	0.2239
46	1.2253	1.13	0.1253
47	0.7782	0.998	-0.2198
48	1	0.97	0.026
49	0.9546	0.97	-0.0197
50	0.7782	0.97	-0.1958
51	1.8865		
52	1.5441	1.422	0.1221
53	1.5185	1.422	0.0965
54	1.0414	1.027	0.0144
55	1.6021	1.54	0.0621
56	0.9031	1.298	-0.3949
57	0.7782		
58	1.4472	1.358	0.0892
59	1.14314	1.24	0.1772
60	1.6021	1.483	0.1191
61	0.6989	1.029	-0.3301
62	0.6989	0.98	-0.2811
63	0.4772	0.402	0.0752
64	1.7161	1.037	0.1391
65	0.6989	0.903	-0.241
66	0.7782	0.877	-0.0988
67	0.9031	0.877	0.0261
68	0.6021	0.877	-0.2746
69	1.8751		
70	1.4771	1.331	0.1661
71	1.4772	1.331	0.1462
72	0.9542	0.944	0.0102

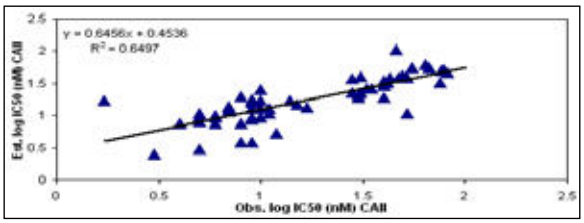

Figure: - Comparison of observed & estimated log IC50 (nM) CAII using model – 15.

Conclusion:-

On the basis of above rending we conclude that Log IC50 (CAII) activity can be modeled using the physicochemical parameters MW, MR, n, d & IP5 has been found to be excellent. Our result better then the earlier reported results.

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