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QSPR STUDY OF A GROUP OF 1,3,4 THIADIAZOLE AND 1,3,4 THIADIAZOLINE DISULFONAMIDS WITH BIOLOGICAL ACTIVITY LOG HCA 1

KEYWORDS

Qspr Study Of A Group Of 1,3,4 Thiadiazole And 1,3,4 Thiadiazoline Disulfonamids With Biological Activity log HCAI.

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ABSTRACT *In the present investigation the applicability of various physicochemical parameters are tested for the QSPR study on 1,3,4 Thiadiazole and 1,3,4 Thiadiazoline Disulfonamides, the regration analysis shown that even in the multi parameters correlation of physicochemical parameters give singificant regration coefficiant further more writing combination of physicochemical parameters along with the indicater parameters, a tremendous improvement in the statistics has been observed the result are critically discussed on the basis regration data.*

INTRODUCTION –

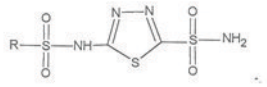
Quantitative structure- property-activity relationship (QSPR/ QSAR) have been stablished as powerful research tool & are being used in many fields, there are mathematical models in that property & activities of molecules are predicted from their structure 1,3,4 Thiadiazole-2 Sulfonamide and there derivatives are used for clinical purpose. They are being used age divureties [8-11], antiglucoma agents, anti epilopic agents [14] and anitiulcer agents[15].

The major biological activity of acetazolamide and related hetrocyclic/ aromatic sulfonamides is connected with the powerful inhibition of the zinc enzyme carbonic anhydrase [16-20].

Supram et al[21]. have reported Quantum chemical QSAR of a group of 1,3,4 diazole and 1,3,4 thiadiazoline disulfonamides with carbonic anhydrase inhibitory properties.

Agrawal and Khadikar [22] have used topological indices for modeling inhibitory activity of various CA inhibitors. they also proposed statistically significant models for modeling estimating and predicting in inhaibitory activities of CA-inhibitors.

The general structure of CA inhibitors used in our work are given below :-



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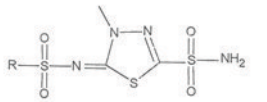

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Materials & Methods -

The study was carried on the compounds prepared by supuran et al they have used activities of a group of 1,3,4 Diazole and 1,3,4 Thiadiazolene disulfonamides with Log HCAI.

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), Parachor(PR), Surface Tension(γ), Density (D), Polarizability () & index of refraction (N), The calculation of parameters for all 40 compounds.

Correlation Matrix

We have studied the inter correlation of the parameters along with the biological activity & indicator parameters, parameters MW, MR, MY, PR and are the parameters which show good correlation with IC50 (nm) (Log HCAI) inhibitory activity.

Result & Discussion -

A set of 40 Thiadiazole and Thiadiazoline disulfonamides with Carbonic Anhydrase inhibitory properties are taken from the work of Supran et al[22]. The structural details of these compounds along with their biological activities log HCAI are reported table. This table also records the value of three indicators parameters which are dummy parameters responsible for substitution at R, IP, has been taken as unity if the compounds belong C type. IP2 has been taken as unity if the compounds belong to E type and IP3 is taken as unit if R vis mono substituented on all other cases they are given zero value.

Parameters which can be used for modeling the log (CAI) activity the multi parameteric.

Then a seven parametric correlation is found to be the best Result R = 0.9232 this model includes on addistional parameters . Figure 1 -

Log HCAI = -0.002 (0.0012) MW+ 6.4931 (5.4735)
MR-0.0711 (0.0272)MV +9.8592 ´ 10^{-4} ($5.6966´10^{-4}$)
PR-18.3297 (6.061) N-158752 (13.8278)
-0.1956(0.8160)IP3+30.9474
N=40 Se= 0.2172 R = 0.9232 F = 23.081 Q = 4.2505

Compd. No.	Observed (HCAI)	log IC50 (nM) (HCAI)	
		Model- 24	Residue
1.	1.0000	0.7820	0.2180
2.	0.8451	1.0390	-0.1939
3.	0.6989	0.8040	-0.1051
4.	0.602	0.8340	-0.2320
5.	0.6021	0.7440	-0.1419
6.	0.4771	0.5680	-0.0909
7.	0.6989	0.8880	-0.1891
8.	1.0000	0.9110	0.0890
9.	0.7782	0.6260	0.1522
10.	0.9542	0.8580	0.0962
11.	0.4741	0.6860	-0.2119
12.	0.3010	-	-
13.	0.6989	0.9180	-0.2191
14.	1.2787	0.9420	0.3367
15.	0.0000	-	-
16.	1.2553	0.9960	0.2593
17.	2.5563	2.5770	-0.0207
18.	1.0792	0.9370	0.1422

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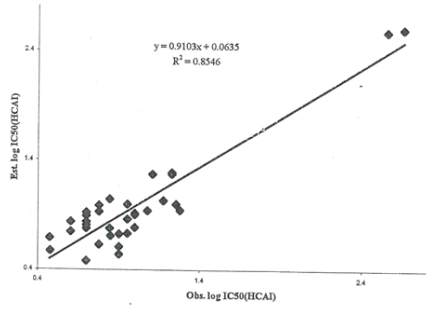
19.	0.9542	0.9940	-0.0398
20.	1.1761	1.0300	0.1461
21.	1.2304	1.2880	-0.0576
22.	0.7782	0.9830	-0.2048
23.	0.6989	0.8330	-0.1341
24.	0.9031	0.6070	0.2961
25.	0.9030	0.7220	0.1810
26.	0.6989	0.4780	0.2209
27.	0.7782	0.9260	-0.1478
28	0.3010	-	-
29.	0.0000	-	-
30.	0.0000	-	-
31.	0.9031	0.5400	0.3631
32.	0.8451	0.7720	0.0731
33.	0.6989	0.7720	-0.0731
34.	0.9542	0.7280	0.2262
35.	0.0000	-	-
36.	1.2304	1.2740	-0.0436
37.	2.6580	2.6010	0.0570
38.	1.0000	0.8980	0.1020
39.	0.8500	0.7050	0.1450
40.	1.1100	1.2710	-0.1610

Graph-



Comparison of observed and estimated log IC50 (nM) (HCAI) using model.

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