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Study of hCA-(II) inhibitory activity of o-,m- & p- amine benzene sulphonamide by some topological indices

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Abstract

The paper deals with an inhibitory effect against Human Carbonic Anhydrase (hCA) using some topological indices on o-,m- & p-amine benzene sulphonamide. In this paper, we restrict ourselves on connectivity-based indices viz. Balaban Index(J), Balaban related index (F &G), R (cyclomatic number) and $^1\chi$(Randic-connectivity index).

Introduction

Carbonic anhydrases (CA's) are important metalloenzymes found in red blood cells,gastric mucosa,pancreatic cells and renal tubes.They are responsible for the intervention of carbonic acid and CO_2 to HCO_3^- and H_3O^+, playing an important role in several physico-pathological processes that include the transport of carbon dioxide, the formation of HCl in the stomach and elevated pressure of aqueous humour in eye(glaucoma).[1-5]

The reaction catalysed by carbonic anhydrase is :

$$H_2CO_3 \xrightleftharpoons{CA} CO_2 + H_2O$$

As it removes a water molecule from carbonic acid ,so named carbonic anhydrase(CA).

Methodology: Topological indices are the number reflecting certain structural features of any molecule that are obtained from the respective molecular graph. Structural information described in a molecular graph are quantified in the form of topological indices. The first topological index "w"was introduced by Harold Weiner[6] and bear his name.Later on, Haruo Hosoya[7] advanced his index z, and introduced the name topological index.

Supuran and co-workers[6,8-9] has done extensive work on CA inhibition and is considered as a pioneer worker in this field. Although many topological indices have been proposed, we shall discuss here only Balaban index[10-12] and Randic connectivity index:

(1)Balaban index: The average distance based connectivity index J, known as Balaban index uses distasums instead of vertex degrees and is averaged by the number 'E'of edges and by the cyclomatic number (conventional number of rings) *i.e.* R=E-N+1, where R is a

cyclomatic number & N is the number of graph vertices. It has lower degeneracy than all previous topological indices[13]. Index 'J' increases appreciably with branching ,but the very slight increase with graph size is limited asymptotically. For infinite path, it's value is the number π=3.14159….. Because index 'J' is normalized for graph size, it should not be used in mono-parametric correlation with properties where the molecular size accounts for a significant part of the variance.

$$J = [E(R+1)]\Sigma all\ edges(s_i \times s_j)^{-0.5}$$

For those properties where not only the "shape" but also the size of the graph influence the property/activity, two indices related to 'J' have been developed. The first of these index is F, defined as;

$$F = E\ \Sigma all\ edges(s_i \times s_j)^{-0.5} = J(R+1)$$

This index is able to separate graph size, cyclicity and branching.[14]

The other J-related index 'G' is more convenient for correlations. It is defined as[14]

$$G = \left[\frac{n^2 E}{n+R+1}\right] \Sigma_{all\ edges}(s_i \times s_j)^{-0.5}$$

$$= \frac{n^2(R+1)}{n+R+1} = \frac{n^2 F}{n+R+1}$$

(2)First –order connectivity index ($^1\chi$)*:* The connectivity –index graph ($^1\chi$) of a graph G is defined by Randic as under[15,16]

$$^1\chi = \chi(G) = {}^{\Sigma}{}_{i}{}^{\Sigma}{}_{j}\delta i\ \delta j]^{-0.5}$$

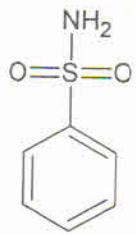
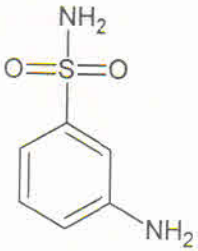
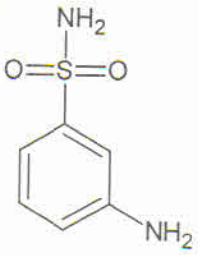
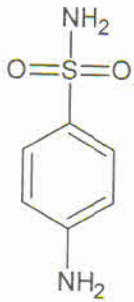
The methodology used in present investigation is to calculate the CA(II) inhibitory activities of CA-inhibitor which are taken from literature[17-19]

And the topological indices are calculated using the software Dragon[20].

Observation

Structures of the studied substituted amine benzene sulphonamides are shown in Table 1 .

Table 1

 Benzene sulphonamide	 o-amine benzene sulphonamide	 m-amine benzene sulphonamide	 p-amine benzene sulphonamide

The calculated values of Balaban (J) and it's related index (F &G) with Randic connectivity index ($^1\chi$) are given in Table 2.

Table 2

Name of the compound	Binding const (log K_i)	R	J	F	G	$^1\chi$
o-amine benzene sulphonamide	2.4699	1	2.545	5.09	47.376154	5.016
m-amine benzene sulphonamide	2.3802	1	2.461	4.922	45.812461	4.999
p-amine benzene sulphonamide	2.4771	1	2.394	4.788	44.565231	4.999

Discussion

A perusal of Table 2 reveals that the inhibition values are in compliance with the fact that $-NH_2$ group activate the o- & p-position while deactivate at m- position. The highest inhibition value at p-position is due to least steric hindrance. As the value of 'J' decreases, the inhibition values increases. Lesser value of 'J' refers to greater distance between amino and sulphonamide group. 'R' is a cyclomatic number and it's value is unity for all substituted amino benzene sulphonamide. Indices 'F' and 'G' (the related indices) shows the same order as that of 'J'.Randic connectivity index ($^1\chi$) values are almost the same for o-, m- ,and p- position which clearly shows that it is independent of the position of substitution.

Conclusion

Balaban and Balaban related indices are in support of the fact that $-NH_2$ group activates the benzene ring at o- and p- positions.

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