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The Development of Pharmacophore Model of Sulfocoumarins (1,2-Benzoxathiine-2,2-Dioxides is a Potent Inhibitors of Tumor-Associated Carbonicanhydrases

Shalini Singh[1*], Deepa Singh[1], Ajay Kumar Singh[2] and Poonam Shukla[3]

[1]QSAR and Cheminformatics Laboratory, Department of Chemistry, India

[2]Department of Physics, Bareilly College, India

[3]Department of Chemistry, Ara University, India

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Corresponding author:
Shalini Singh,
QSAR and Cheminformatics Laboratory, Department of Chemistry, Bareilly College, Bareilly, India, Tel: +91- 9412866221;
Email: shalinisingh_15@yahoo.com

ABSTRACT

Coumarins are a novel class of Carbonic Anhydrase inhibitors. Accordingly, Sufocoumarins also act by the same mechanism and act as effective CA inhibitors. Sulfocoumarins are hydrolyzed by esterase CA activity to 2-hydroxyphenyl-vinyl sulfonic acids which bind to the enzyme in a region rarely occupied by other classes of CA inhibitors.

INTRODUCTION

Coumarins are structurally related to lactones and can be prepared from Salicylaldehyde by Perkin Reaction (reaction with acetic anhydride + Sodium acetate) or by Pechmann Condensation in which resorcinol and ethyl acetoacetate are made to react in presence of Polyphosphoricacid (PPA). Coumarin such as 1, a natural product obtained from the Australian plant Leionemaellipticum, (of Rutaceae family) or the simple unsubstitutedcoumarin2 have been found to act as effective inhibitors of the metalloenzyme, Carbonic Anhydrase (CA, EC 4.2.1.1) [1-3]. Coumarins such as Sulfocoumarins (1,2-benzoxathiine 2,2-dioxides) have been demonstrated to possess versatile, effective and isoform selective properties of inhibition of tumour related, hCA IX and XII, as reported by Supuran et al [4] Carbonic Anhydrases are ubiquitious by their presence in the whole animal kingdom, right from the lowest class bacteria, algae to the top order vertebrates like mammals. Carbonic anhydrases are involved in a variety of physiological processes including respiration and transport of CO2 and /or bicarbonate between tissues and lungs in the body and maintain pH in the metabolizing tissues. Zinc atom in II oxidation state is present in the Carbonic Anhydrase which thus, facilitates the process of respiration in animals [5-6].

$CO_2 + H_2O \longleftrightarrow HCO_3^- + H^+$

In mammals 15 different kinds of CA isozymes and CA-related proteins (CARP) are present in different isoforms of which 11 are catalytically active:

(1) Cytosolic forms	(CAI,CAII,CAIII,CAVII)
(2) Membrane- bound	(CAIV,CAIX,CAXII,CAXIV) isozymes
(3) Mitochondrial forms	(CA VA and VB)
(4) Saliva /Milk	(CAVI)

Inhibition as also the activation of these enzymes may be exploited clinically in the treatment or prevention of variety of disorders such as glaucoma, epilepsy, obesity and gastric ulcers etc. In Pharmaceutical chemistry, the rational drug design for human health hazard and environmental risk assessment purposes, several statistical mathematical techniques are employed to unravel information obtained.

CONCLUSION

In this paper we present the Pharmacofore model and protein acceptor structure of sulphocumarin. Sulphocumarin, which is a substitute for cumarin, (cumarin is a product of a medicinal plant)in its structure in the (Figure 1). The computer developed representation of the pharmacophore model: This also includes information on the available space at important substituent positions. Figure 1 represents pharmacophore models with most active compound which is generated by Brood. The model displays seven pharmacophore elements (hydrogen bond acceptors) which are used to develop and describe the interaction between ligands and the target receptor from the ligand point of view and (Figure 2) shows the area of protein acceptor (Figure 3).

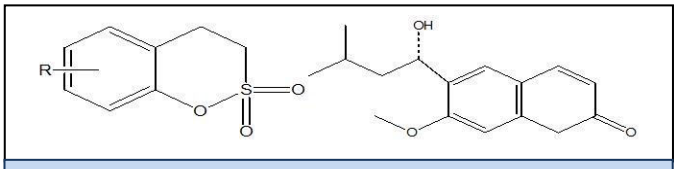

Figure 1: Structure of Sulphocoumarin Structure of Coumarin.

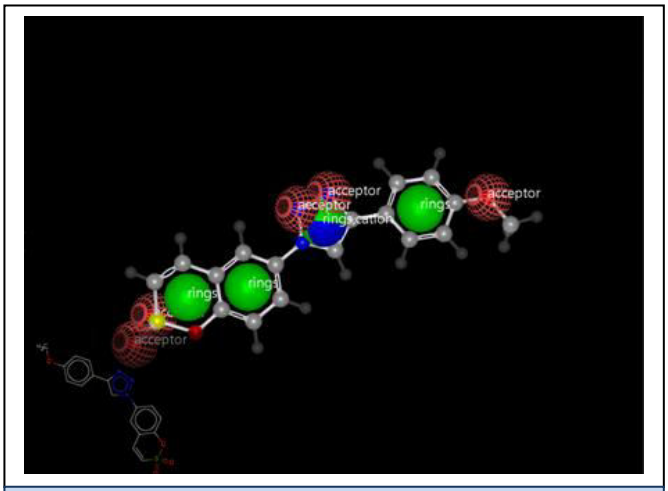

Figure 2: Pharmacophore model.

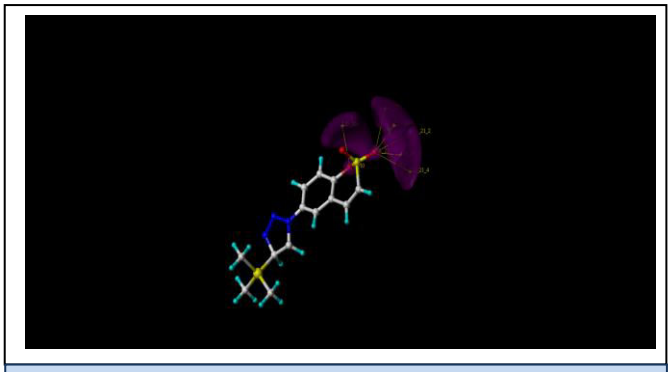

Figure 3: Protein acceptor

REFERENCES

1. Vu H, Pham NB, Quinn RJ. (2008). Direct screening of natural product extracts using mass spectrometry. J Biomol Screening. 13: 265-275.
2. Maresca A, Temperini C, Pochet L, Masereel B, Scozzafava A, et al. (2010). Deciphering the mechanism of carbonic anhydrase inhibition with coumarins and thiocoumarins. J Med Chem. 53: 335-344.
3. Maresca A, Supuran CT. (2010). Coumarins incorporating hydroxy- and chloro- moieties selectively inhibit the transmembrane, tumor-associated carbonic anhydrase isoforms IX and XII over the cytosolic ones I and II. Bioorg Med Chem Lett. 20: 4511-4514.
4. Tars K, Vullo D, Kazaks A, Leitans J, Lends A, et al. (2013). Sulfocoumarins (1,2-Benzoxathiine-2,2-dioxides): A Class of Potent and Isoform,A. Selective Inhibitors of Tumor-Associated Carbonic Anhydrases. J Med Chem. 56: 293-300.
5. Mincione F, Menabuoni L, Supuran CT. (2004). Clinical applicationsof the Carbonic anhydrase inhibitors in ophthalmology. In:Supuran C, Scozzafava A, Conway J, editors. Carbonic anhydrase, its inhibitors and activators. Boca Raton (FL):CRC Press. p243-254.
6. Supuran CT, Scozzafava A, Conway J (eds). (2004). Carbonic anhydrase–its inhibitors and activators. Boca Raton (USA):CRC Press. p1-363.