APPENDIX A

Animal ethics

ANIMAL ETHICS COMMITTEE

Central Animal House Registration No: 769/2011/CPCSEA

1. Title of project: ***Design,Synthesis and Characterization of new Diarylsulfonylurea-chalcone Hybrids as Potential anti-Inflammatory agents***
2. Authors: **Bharat Kumar Bugata**
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Date: 14/10/2013.

Sigma Institute of Clinical Research & Administration Pvt. Ltd. HYDERABAD

Chair person 14/10/13.
Animal ethics committee
SICRA labs Pvt Ltd.

Research Article

QSAR and Docking Studies of Synthesized Diarylsulfonylurea Chalcone Hybrids as Anti-Inflammatory Agents

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ABSTRACT

The synthesis of a series of Diarylsulfonyl ureas Chalcone Hybrids is used to be evaluated for their anti-inflammatory activity using *in silico* methods. The activity of Diarylsulfonylurea Chalcone Hybrids using 2D Qsar and docking studies (Hex and igemDock) has been not reported till now. In the present studies, QSAR properties has shown higher molecular surface with 4e followed by 4u, 4c, 4i and 4d. Parameters like Volume, Refractivity, Polarizability and Mass has obtained more for 4y, Hydration energy is more with logP and less for 4m. The most five preferable structures (4f, 4g, 4m, 4u and 4v) having least minimization energies with docked structural comparison using hex v6.3. The five preferable structures (4a, 4b, 4e, 4s and 4y) has least minimization energies with the active binding sites and docked Structural Comparison using iGEMDOCK. Hence the proposed work has shown good anti-inflammatory activity with Synthesized Diarylsulfonylurea Chalcone Hybrids using *in silico* studies.

Keywords: Anti-inflammatory activity, Docking, QSAR, Synthesized Diarylsulfonylurea Chalcone Hybrids.

INTRODUCTION

Chalcones, a new class of glycosidase (α-glucosidase, α-amylase, and β-amylase) inhibitors acts against α-glucosidase shows non-competitive inhibition.[1] The effect of chalcones on serum glucose-lowering in hyperglycemic-normal rats highlighting novel compounds with strong anti-hyperglycemic properties.[2] Chalcones, considered as the precursors of flavonoids and isoflavonoids, area unit galore in edible plants, and have conjointly been shown to show a various array of medical specialty activities.[3]

Chalcones represent a vital cluster of the polyphenolic family, which incorporates an outsized variety of present molecules. This family possesses a stimulating spectrum of biological activities, as well as antioxidative, medication, medicament, anticancer, cytotoxic, and immunosuppressive potential.[4] Conversion of the difluorinated chalcones to difluorinated propanediones seems to provide better protection against inflammation.[5] The substitution of an aryl group of chalcone by a heterocyclic quinoline group would enhance the biological activity.[6]

The sulfonylurea, inhibits eosinophil survival in a manner similar to lidocaine.[7] Sulfonylurea's include several medications that act on β-cells to increase insulin release.[8] Diarylsulfonylurea (DSU) is a novel anticancer agent because of its unique DSU chemical structure, broad-spectrum antisolid-tumor activity in preclinical models.[9] DSUs with exceptionally broad-spectrum activity against syngeneic rodent solid tumors *in vivo* is described.[10]

Quantitative structure activity relationship (QSAR) approach is better for designing new drugs when the target is not known or if there are multiple targets.[11] The anticancer result of chalcones derivatives and new QSARs are able to facilitate within the understanding of the role of chalcones and of their analogues on cancer.[12] From the QSAR studies, Pharmacophores has been established for coming up with novel medication molecules.[13]

Sulfonylurea were the only drugs used to stimulate insulin secretion in patients with type 2 diabetes.[14] A need for rapid and efficient computational methods capable of differentiating compounds with acceptable biopharmaceutical and QSAR properties.[15]

Methodology

A series of new Diarylsulfonylurea-Chalcone hybrids compounds (4A-4y) has been studied by QSAR through Hyperchem v5.1 software. The compounds synthesized by Bharat *et al,* 2013 has been analyzed for anti-inflammatory activity through *in vitro* studies.[16]

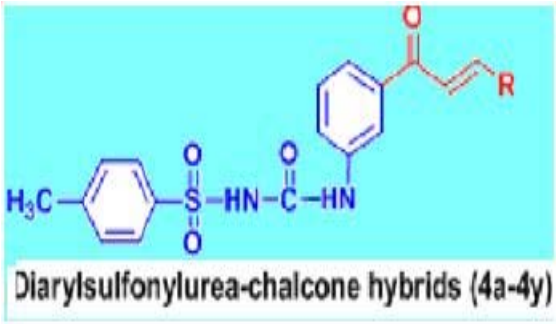

Figure 1: Diarylsulfonylurea-chalcone bioactive pharmacophores

Protein related to anti-inflammatory activity of 5-LOX inhibitor has been retrieved from PDB (3V99) and has been used as receptor. Various ligands have been designed using Chemdraw ultra v10.0 and the 3D models are subjects to energy minimization using molecular