Achaiah Garlapati, J Diabetes Metab 2018, Volume 9
DOI: 10.4172/2155-6156-C3-084

New Thiazolidine-4-Ones: Synthesis And Evaluation For Antidiabetic Activity

Achaiah Garlapati
Kakatiya University, India

Statement of the Problem: 1,3-Thiazolidindiones (TZDs) are important class of antidiabetic agents which enhance insulin sensitivity of the target cells via activation of Peroxisome Proliferator-Activated Receptor gamma (PPAR-γ), a nuclear receptor involved primarily in glucose homeostasis, adipogenesis, inflammatory diseases and certain types of cancers.1,3-Thiazolidindiones are associated with various untoward effects, restricting their usage in the treatment of Type 2 diabetes. The main side effects of all TZDs are water retention, heart failure. Therefore, TZDs should be prescribed with both caution and patient warnings about the potential for water retention/weight gain, especially in patients with decreased ventricular function. The two TZDs, pioglitazone and rosiglitazone, are PPAR-γ agonists, do not cause serious liver damage, but do induce weight gain, fluid retention and heart failure and they have been associated with an increase in peripheral fractures in postmenopausal women, particularly in the humerus, hands and feet. Furthermore, it has been established that selective activation of PPAR-γ sub-type is primarily responsible for the observed undesirable effects. Therefore, partial agonists are considered a safer alternative to currently used thiazolidinediones (TZDs). The attempt to develop such molecules, several modifications have been attempted in the tail and head groups of the TZDs to result in thiazolidin-4-ones and a few of them have been identified to possess potential antihyperglycemic activity. The purpose of this study is to synthesize and screen new derivatives (General Structure) obtained by the incorporation of pyridine/pyrimidine in the tail and thiazolidine-4-one with cyclopropyl, alkyl, aryl groups etc. In place of R group and methyl and hydrogen in place of R1. Methodology: 4-[2-(Methyl-pyrimidin/pyridin-2-yl-amino)-ethoxy]-benzaldehyde (2) was prepared from 2-(methyl-pyrimidin/pyridin-2-yl-amino)-ethanol (1) and 4-fluorobenzaldehyde. The compound 2 in turn treated with appropriate amine and thioglycolic acid/ thiolactic acid to get the thiazolidine-4-ones. Findings: All the seven target molecules showed significant reduction in blood glucose levels in the streptozotocin induced diabetic rats at 4^{th} and 6^{th} Hrs after administration. Among the series, the compound with cyclopropyl group and pyridine moiety (IIg) showed comparable potency to that of the standard piogliazone at 6^{th} hour (~55% reduction). Further, the activity increased with % reduction in blood glucose levels reaching 65.75 at 10^{th} Hrs compared to 3% shown by standard indicating prolonged activity by the test compound. Conclusion & Significance: The findings suggest that compound (IIg) could be further modified to improve the potency and tested for toxicity to identify safer molecules for further pre-clinical evaluation.

Biography

Achaiah Garlapati has been working as Professor at Pharmacy institute in Kakatiya university and associated with design, synthesis and screening of various heterocyclic compounds for different biological potencies viz anticancer, anti-inflammatory, antihistaminic, antidiabetic and antimicrobial activities. He guided several PhD students and project work as number of post-graduate students. Some of the compounds synthesized were found to more potent than the existing drug molecules. The results are published in several peer reviewed journals.

achaiah_g@yahoo.co.in

Notes: