SYNTHESIS, BIOLOGICAL EVALUATION, DOCKING AND QSAR STUDIES OF SOME NOVEL THIAZOLIDINEDIONES AS PARTIAL PPARΓ AGONISTS

[1]KALPANA TILEKAR, [2]NEHA UPADHYAY, [3]PRAMOD KUMAR GUPTA, [4]VIRUPAKSHA A. BASTIKAR, [5]C. S. RAMAA

[1,2,5]Department of Pharmaceutical Chemistry, BharatiVidyapeeth's college of Pharmacy, CBD Belapur, Navi Mumbai-400614, Maharashtra, India
[3]School of Biotechnology and Bioinformatics, D YPatil University, Navi Mumbai, Maharashtra, India
[4]Amity Institute of Biotechnology, Amity University, Mumbai, Maharashtra, India
E-mail: [5]sinharamaa@yahoo.in

Abstract - Apart from their known antidiabetic activity, the ability of Thiazolidinediones (TZDs) to contribute to cancer therapy has been evidenced by numerous in vitro and in vivo studies. While TZDs are known to stimulate PPAR-g receptor, they also have multiple PPARγ independent effects and the specific role of PPARγ activation in the anticancer effects of TZDs is still under investigation. This prompted us to develop TZD analogs and evaluate their anticancer potential.
In the present work, 25 novel derivatives of 5-benzylidene-2,4-thiazolidinediones were synthesized and their structures were determined by analytical and spectral (FTIR, 1H NMR, 13C NMR) methods. The newly synthesized compounds were evaluated for their antiproliferative activity. Though the compounds showed varying degrees of cytotoxicity in the tested cell lines, most marked effect was observed in MCF7 (breastcancer), K562 (leukemia) and GURAV (nasopharyngeal cancer) cell lines.The docking study was performed usingVLife protocol. It was found that most of the synthesized compounds interact with the same binding as that of partial agonists of PPARγ. The QSAR study was performed using VLife Software. QSAR model was developed and validated for activity on K562 cell lines.It should be noted that the predicted activities by our QSAR models were very close to those experimentally observed, indicating that these models can be safely applied for prediction of more effective hits having the same skeletal framework.

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