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5-naphthylidene-2,4-thiazolidinediones: *In silico* studies, synthesis and primary cytotoxicity evaluation in leukemic cell lines

Neha Upadhyay¹, Kalpana Tilekar¹, Piotr Mrowka², Pramodkumar Gupta³, Virupaksha A Bastikar⁴, Kaustubh Wagle¹ and C S Ramaa¹¹Bharati Vidyapeeth's College of Pharmacy, India²Medical University of Warsaw, Poland³D Y Patil University, India⁴Amity University, India

Introduction: Contribution of antidiabetic Thiazolidinediones (TZDs) to cancer therapy has been evidenced by numerous *in-vitro* and *in-vivo* studies. While TZDs are known to stimulate PPAR- γ receptor, they also have multiple PPAR γ independent effects and the specific role of PPAR γ activation in the anticancer effects of TZDs is still under investigation. Also, several reports show the correlation between full activation of PPAR γ and associated adverse effects. This prompted us to develop TZD analogues as partial PPAR γ agonists and evaluate their anticancer potential.

Methods: We designed series of novel TZDs based on, QSAR model, Docking analysis and Molecular properties study. Further we synthesized and structurally characterized them by ¹H-NMR, ¹³C-NMR, FTIR and Mass spectroscopy.

Results & Discussion: In the present work, a QSAR model was developed and validated using 25 TZD derivatives synthesized in our laboratory earlier, showing antiproliferative activity against K 562 cell lines, by using experimental and computational study and analysis. 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. We used this model to design new series of 5-naphthylidene-2,4- TZDs and predicted their antiproliferative activity. The molecules from the series, obeying Lipinski's rule of five were subjected to docking analysis using VLife protocol. The molecules displaying desired interactions as that of partial agonists of PPAR γ were further taken for synthesis and evaluated for primary cytotoxic effects on several cancerous cell lines.

Biography

Neha Upadhyay has completed her Post-graduation in Pharmaceutical Chemistry from Bombay College of Pharmacy, Mumbai. She is working as a Junior Research Fellow (JRF) on a project funded by DST, India. She has registered for PhD in Pharmaceutical Sciences at Bharati Vidyapeeth's College of Pharmacy, Navi Mumbai, India.

upadhyayneha16@gmail.com

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