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Synthesis, biological evaluation and molecular simulation studies of new arylated benzo[h]quinolines compounds as potential anticancer agents

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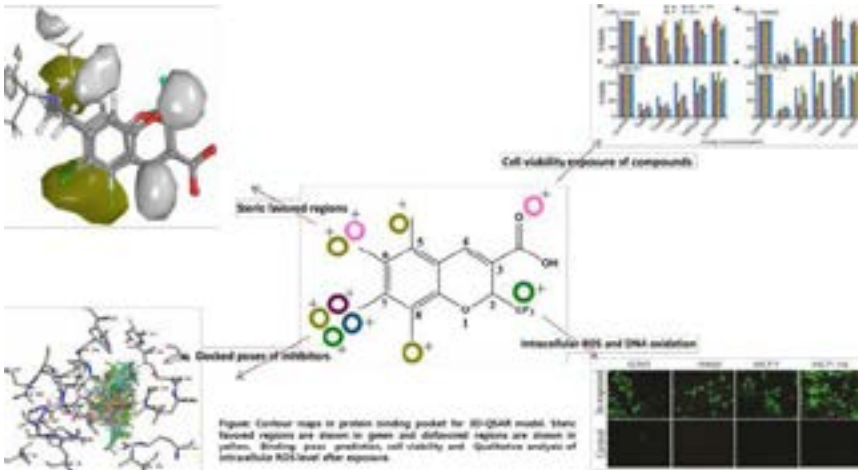
In this study, we have carried out Gaussian-based 3D-QSAR model against the target COX-2 with good statistical significance (R2training=0.86) and predictability (Q2training=0.66, Q2test=0.84). The 3D-QSAR includes steric, electrostatic, hydrophobic and hydrogen bond acceptor field indicators, whereas the potential field contributions indicate that the steric and hydrophobic features of the molecules play an important role in governing their biological activity. The anti-cancer activity of the benzo[h]quinolines was evaluated on cultured human skin cancer (G361), lung cancer (H460), breast cancer (MCF7) and colon cancer (HCT116) cell lines. The inhibitory effect of these compounds on the cell growth was determined by the MTT assay. Among the synthesized compounds 3e, 3f, 3h and 3j showed potential cytotoxicity against these human cancer cell lines. Effect of active compounds on DNA oxidation and on expression of apoptosis related gene was studied. While their bioavailability/drug-likeness was predicted to be acceptable but requires future optimization. These findings reveal that benzo[h]quinolines act as anti-cancer agents by inducing oxidative stress-mediated DNA damage. Molecular simulation study was performed to find binding conformations and different bonding behaviors, in order to reveal the possible mechanism of action behind higher accumulation of active benzo[h]quinolines with β-tubulin.

Recent Publications

- Yadav DK, Kumar S, Saloni, Singh H, Kim MH, Sharma P. Misra S, Khan F (2017) Molecular docking, QSAR and ADMET studies of withanolide analogs against breast cancer. Drug Design, Development and Therapy 11:1859-1870.
- Yadav DK, Rai R, Kumar N, Singh S, Misra S, Sharma P, Shaw P, Pérez-Sánchez H, Mancera RL, Choi EH, Kim MH, Pratap R (2016). New arylated benzo[h]quinolines induce anti-cancer activity by oxidative stress-mediated DNA damage. Scientific reports 6:38128.
- Yadav DK, Dhawan S, Chauhan A, Qidwai T, Sharma P, Bhakuni RS, Dhawan OP, Khan F (2014). QSAR and docking based semi-synthesis and *in vivo* evaluation of artemisinin derivatives for antimalarial activity. Current Drug Target 15(8):753-61.
- Yadav DK, Ahmad I, Shukla A, Khan F, Negi AS, Gupta A (2014). QSAR and docking studies on Chalcone derivatives for anti-tubercular activity against M. tuberculosis H37Rv. Journal of Chemometrics 28: 499-507
- Yadav DK, Kalani K, Singh AK, Khan F, Srivastava SK, Pant AB (2014). Design, synthesis and *in vitro* evaluation of 18β-glycyrrhetinic Acid derivatives for anticancer activity against human breast cancer cell line MCF-7. Curr Med Chem 21(9):1160-70



Biography

Dharmendra K Yadav received his PhD degree from CSIR-Central Institute of Medicinal and Aromatic Plants, Lucknow, India, in 2013. During Doctoral research, he focused on the Molecular Modeling and Drug Design. After completion of PhD, he moved to Hanyang University Seoul, Korea for Postdoctoral Research and worked on QNTR. During this period he had performed his research in Molecular Modeling on nanoparticles specially using QNTR, etc. After completion, he moved to University of Delhi and All India Institute of Medical Sciences, Jodhpur, India. He has published more than 38 research papers in reputed international journals with high impact factor and has one US patent. He is continuing his research in Computer-Aided Drug Design Dynamics Simulation of Biological Networks and Plasma Medicine, etc.

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