ORIGINAL RESEARCH ARTICLES

STRUCTURE-BASED DESIGN, *IN SILICO* ADME, SYNTHESIS AND *IN VITRO* PHARMACOLOGICAL SCREENING OF COUMARIN CHALCONE ANALOGUES AS EGFR INHIBITORS FOR NON-SMALL CELL LUNG CANCER

Archanadevi A. Patel[a] and Archana S. Gurjar[a]*

(Received 03 December 2024) (Accepted 08 March 2025)

ABSTRACT

Non-small cell lung cancer (NSCLC) primarily reveals overexpression of epidermal growth factor receptors (EGFR), driving uncontrolled and abnormal cell divisions in lung tissue. Gefitinib is a first-generation EGFR inhibitor that is widely used as first-line NSCLC treatment, hence PDB ID 4I22 was selected with gefitinib as co-crystallized ligand. A series of coumarin chalcone analogues were designed and investigated as EGFR inhibitors using molecular docking and also subjected to *in silico* ADME studies. In molecular docking, some analogues exhibited good interactions within active site of EGFR (PDB ID 4I22). The analogues with favorable computational results were considered further for synthesis and characterized by spectral techniques, IR and ^{1}HNMR. These synthesized compounds were pharmacologically screened for their anti-proliferative activity. In MTT assay, CC_33 has showcased potent cytotoxicity on cell line NCI-H23 (IC_{50}: 45.277 µM) relative to gefitinib (IC_{50}= 12.904 µM). Computational findings align with cell line studies, identifying promising analogues as potential leads to target specifically NSCLC.