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Research Article

Molecular dynamic simulations based discovery and development of thiazolidin-4-one derivatives as EGFR inhibitors targeting resistance in non-small cell lung cancer (NSCLC)

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Abstract

Targeting kinases with oncogenic driver mutations in malignancies with allosteric kinase inhibitors is a promising new treatment technique. EGFR inhibitors targeting the L858R/T790M/C797S mutation bearing thiazolidine-4-one scaffold were discovered, optimized, synthesized, and biologically evaluated. According to *in silico* and *in vitro* studies, compounds **6a** and **6b** resulted to be highly potent with IC_{50} values of 120 nM and 134 nM and good selectivity. Compound **6a** displayed significant antioxidant activity, with a DPPH radical scavenging value of 92.15%. The potency of compounds was also compared with ADMET and molecular dynamics simulations study. A comparative simulation of model protein and protein-ligand complex in presence and absence of compound **6a** has been carried out.

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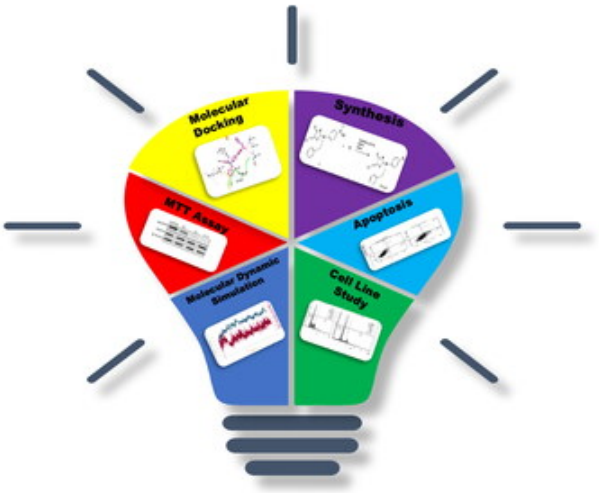

Keywords: EGFR allosteric thiazolidine-4-one ADMET molecular docking molecular dynamic simulations

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Disclosure statement

The authors report no conflicts of interest in this work.

Data availability statement

The data that support the findings of this study are available from the corresponding author, P.S.W, upon reasonable request.

PDB codes

PDB ID: 5D41.

Additional information

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