link: https://www.tjnpr.org/index.php/home/article/view/7654

Molecular Docking and Dynamics Simulation of *Holothuria scabra* In Non-Small Cell Lung Cancer Through Inhibition of EGFR and KRAS Pathways

Authors

- **Ikhwandi C. Nugraha**School of Medicine, Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Makassar, Makassar, Indonesia 90221
- **Ami Febriza**Physiology Department, Faculty of Medicine and Health Sciences, Universitas Muhammadiyah Makassar, Makassar, Indonesia 90221

DOI:

https://doi.org/10.26538/tjnpr/v9i10.50

Keywords:

Kirsten Rat Sarcoma Viral Oncogene Homolog, Epidermal Growth Factor Receptor, Holothuria scabra, Molecular Dynamic, Molecular Docking, Non-Small Cell Lung Cancer

Abstract

Non-small cell lung cancer (NSCLC) is one of the leading causes of cancer-related mortality worldwide, highlighting the urgent need for novel therapeutics to overcome resistance and improve patient outcomes. This study employed an *in silico* pipeline to evaluate the potential of bioactive compounds from *Holothuria scabra* as inhibitors of epidermal growth factor receptor (EGFR) and KRAS, which are key NSCLC drivers. Selected *H. scabra* compounds retrieved from PubChem were screened for toxicity using ProTox 3.0, docked with PyRx/AutoDock Vina against EGFR (PDB: 2ITY) and KRAS (PDB: 7LGI) with Lazertinib as a comparator; the top-ranked complexes were further analyzed through 100 ns molecular dynamics simulations in YASARA (AMBER14/TIP3P) to assess stability. Several *H. scabra* ligands demonstrated stronger docking affinities than Lazertinib (e.g., C3: EGFR ΔG = −9.4 kcal·mol; C4: KRAS ΔG = −8.7 kcal·mol), while toxicity predictions indicated that all compounds were nontoxic. Docking analysis further revealed that compounds C3, C5, and C8 exhibited stronger affinities toward EGFR, with C3 interacting with key binding residues (VAL726, LYS745, and ASP855). Compounds C4, C3, and C7 showed superior affinities for KRAS, with C4 binding to critical residues (LYS117 and LYS147), similar to Lazertinib. Molecular dynamics simulations confirmed that the top ligands, particularly

C3 and C4, maintained stable interactions without inducing significant protein unfolding or persistent root mean square deviation fluctuations. These findings indicate that *H. scabra*-derived ligands, especially C3 and C4, represent promising *in silico* candidates for subsequent biochemical and cellular validation as potential NSCLC inhibitors..