Evaluation of Metabolite Compound of Brown Algae (Sargassum duplicatum sp) and its Anticancer Potential against Lung Cancer Cells: an in vitro, in silico and Bioinformatics study

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ABSTRACT

The high failure rate of lung cancer therapy is primarily attributed to the overexpression of EGFR and HER2. These two biomarkers play a crucial role in lung cancer diagnosis in Indonesia and are frequently observed in lung cancer patients. As a result, efforts to develop novel anticancer therapies continue to advance, particularly to overcome treatment resistance. One promising approach involves secondary metabolites derived from brown algae (Sargassum duplicatum J.Arg.), which have demonstrated potential in inhibiting cancer cell growth. This study evaluates the anticancer activity of brown algae extract (BAC) in A549 lung cancer cells and predicts the molecular targets of its metabolites. The research methodology includes ethanol (70%) extraction of brown algae, gas chromatography-mass spectrometry (GC-MS), bioinformatics analysis of major compounds, molecular docking analysis of EGFR interactions, and cytotoxicity assay, along with gene expression inhibition studies of EGFR and HER2. GC-MS analysis identified 86 bioactive compounds, with hexadecenoic-acid, ethyl ester being the most abundant. Bioinformatics analysis further identified eight molecular targets, with EGFR, ERBB2, and PIK3CA emerging as key genes. Notably, EGFR exhibited the highest degree rank score, indicating strong interactions. Molecular docking analysis revealed that most metabolites interacted more strongly with EGFR than the native ligand, Dacomitinib, with RMSD values below 2Å, suggesting high binding stability. Furthermore, BAC exhibited cytotoxic activity against A549 lung cancer cells and significantly inhibited EGFR and HER2 gene expression. These findings suggest that BAC has strong potential as an effective anticancer agent, particularly in targeting EGFR and HER2 biomarkers.

Keywords: *Sargassum duplicatum J.Arg., lung cancer, EGFR, HER2, bioinformatics*