Investigasi Mekanisme Empon-Empon dalam Pengobatan Hiperinflamasi pada COVID-19 Melalui Pendekatan Bioinformatika = Investigation of the Empon-Empon Mechanism in the Treatment of Hyperinflammation and Covid-19 using a Bioinformatics Approach

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Abstrak

Inflamasi yang tidak terkontrol menjadi penyebab kematian yang signifikan di seluruh dunia dan merupakan faktor penting dalam kasus COVID-19 yang parah. Empon Empon (EE), merupakan jamu tradisional Indonesia secara empiris diyakini mampu menyembuhkan COVID-19 yang parah. Namun, mekanisme kerja senyawa utama dalam mengobati keparahan COVID-19 masih belum jelas. Penelitian ini bertujuan mengidentifikasi senyawa utama EE dan mekanisme molekulernya dalam mengendalikan inflamasi pada COVID-19. Senyawa EE diidentifikasi menggunakan KNApSAcK, protein/target yang terhubung senyawa dikumpulkan menggunakan database: ChemBL, GeneCard, dan Traditional Chinese Medicine Systems Pharmacology (TCMSP), sedangkan target terhubung penyakit dikumpulkan menggunakan GeneCard database. Analisis protein-protein interaction (PPI) dibangun menggunakan String, analisis Gene Ontology (GO) dan Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment menggunakan ShinyGO 0.8. Jaringan interaksi senyawa-target-pathway divisualisasikan dan dianalisis menggunakan Cytoscape 3.10. Analisis penambatan molekul menggunakan PyRx 0.98 serta analisis molecular dynamics simulation (MD) menggunakan NAMD. Diperoleh sebanyak 336 senyawa dalam EE, 28 senyawa diantaranya memenuhi kriteria penyaringan berdasarkan bobot molekul (BM): 200-500 dalton, Oral bioavailability (OB) 30%, drug-likeness (DL) 0.18, tidak menghambat CYP2D6 di hati, toksisitas III. sebanyak 578 target EE diidentifikasi terlibat dalam inflamasi dan COVID-19. Analisis GO dan KEGG mengungkap bahwa aksi farmakologi EE melalui berbagai jalur, termasuk jalur kanker, lipid dan aterosklerosis, serta COVID-19. Analisis PPI diperoleh sebanyak 6 target yang memainkan peran essensial dalam mengendalikan inflamasi dan mengobati COVID-19, yaitu: MAPK3, EGFR, AKT1, PTGS2, TNF dan IL-6. Analisis penambatan molekul menunjukkan bahwa -amyrin, Biochanin-A, Delphinidin, Sesamin, Isorhamnetin, Guaiacin, dan Ellagic acid adalah senyawa yang mampu terikat kuat pada MAPK3, EGFR, AKT1, PTGS2, TNF dan IL-6; hasil ini diperkuat oleh analisis MD yang mengkonfirmasi bahwa interaksi antara senyawa dengan kompleks target esensialnya stabil. Temuan ini memberikan landasan teoritis mekanisme EE dalam mengendalikan inflamasi pada COVID-19, yang dapat digunakan untuk mengembangkan jamu berbasis EE

.....Uncontrolled inflammation is a significant cause of death worldwide and is an essential factor in severe cases of COVID-19. Empon-Empon (EE), a traditional Indonesian herbal medicine, is empirically believed to be able to cure severe COVID-19. However, the mechanism of action of the main compound in treating the severity of COVID-19 is still unclear. This study aims to identify the main compounds of EE and their molecular mechanisms in controlling inflammation in COVID-19. EE compounds were identified using KNApSAcK, and compound-related proteins/targets were collected using ChemBL, GeneCard, and Traditional Chinese Medicine Systems Pharmacology (TCMSP) databases. In a while, disease-linked targets were collected using the GeneCard database. Protein-protein interaction (PPI) analysis was built using String, Gene Ontology (GO) analysis, and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment

using ShinyGO 0.8. The compound-target-pathway interaction network was visualized and analyzed using Cytoscape 3.10. Molecular docking analysis using PyRx 0.98 and molecular dynamics simulation (MD) analysis using NAMD. A total of 336 compounds were obtained in EE, 28 of which met the screening criteria based on molecular weight (BM): 200-500 daltons, Oral bioavailability (OB) 30%, drug-likeness (DL) 0.18, does not inhibit CYP2D6 in the liver, toxicity III. A total of 578 EE targets were identified as being involved in inflammation and COVID-19. GO and KEGG analyses revealed the pharmacological actions of EE through various pathways, including cancer, lipid and atherosclerosis, and COVID-19 pathways. PPI analysis revealed six essential targets in controlling inflammation and treating COVID 19, namely MAPK3, EGFR, AKT1, PTGS2, TNF, and IL-6. Molecular docking analysis showed that -amyrin, Biochanin-A, Delphinidin, Sesamin, Isorhamnetin, Guaiacin, and Ellagic acid were compounds that were able to bind strongly to MAPK3, EGFR, AKT1, PTGS2, TNF, and IL-6; these results were confirmed by MD analysis which confirmed that the interaction between the compound and its essential target complex was stable. These findings provide a theoretical basis for the mechanism of EE in controlling inflammation in COVID-19, which can be used to develop EE-based herbal medicine.