ABSTRAK

Dermatitis kontak adalah peradangan kulit akibat paparan iritan atau alergen, yang memengaruhi 15%-20% populasi global. Penggunaan kortikosteroid topikal adalah terapi utama untuk dermatitis kontak, namun penggunaan jangka panjang dapat menimbulkan efek samping seperti penipisan kulit. Oleh karena itu, diperlukan terapi alternatif yang lebih aman. Kubis (Brassica oleracea) mengandung senyawa bioaktif seperti sulforafan dan Indol-3-Carbinol yang memiliki aktivitas anti-inflamasi dan antioksidan. Penelitian ini bertujuan untuk mengidentifikasi kandungan senyawa aktif dari kubis, menganalisis interaksinya dengan target biologis dalam jalur inflamasi melalui pendekatan *network pharmacology*, serta mengevaluasi potensi anti-inflamasinya melalui *molecular docking* dan pengukuran penghambatan produksi NO pada sel RAW 264.7 menggunakan metode *Griess* untuk membuktikan efektivitasnya sebagai terapi alternatif dermatitis kontak.

Identifikasi metabolit sekunder dilakukan menggunakan Instrumen LC-HRMS. Data spektrum dianalisis menggunakan perangkat lunak *Compound Discoverer 3.3* dengan basis data *mzCloud* dan *ChemSpider*. Studi *network pharmacology* dilakukan menggunakan perangkat lunak *Cytoscape* dengan *plugin ClusterOne* dan *CytoHubba*. Validasi dilakukan melalui *molecular docking* menggunakan *AutoDock Vina*, serta uji *in vitro* pada sel makrofag RAW 264.7 yang distimulasi dengan LPS untuk mengukur kadar *Nitric Oxide* (NO) menggunakan metode *Griess assay*. Data uji *in vitro* dianalisis secara statistik menggunakan *one-way ANOVA*.

Hasil analisis LC-HRMS mengidentifikasi 119 senyawa metabolit sekunder, termasuk *Sulforaphane, Malyngic acid, Indole-3-Carbinol, Iberin, 2-hydroxy palmitic acid, C16 Sphinganine, 1-O-(2R-hydroxy-hexadecyl)-sn-glycerol, N-palmitoyl alanine, Stigmasta-3,5-diene, 1-palmitoylglycerol*. Studi *network pharmacology* mengungkapkan bahwa senyawa-senyawa di atas dapat berinteraksi dengan 13 target protein inflamasi yang terlibat dalam jalur *signaling* terkait dermatitis kontak yaitu TLR4, NFKB1, STAT3, BCL2, PTGS2, EGFR, HSP90AA1, MMP9, TLR2, PPARG, MAPK3, HMOX1, NR3C1. *Molecular docking* menunjukkan energi ikatan senyawa terhadap MAPK3, PTGS2, dan MMP9 berkisar antara -4.06 hingga -7.4 kcal/mol. Uji *in vitro* terhadap sel RAW 264.7 menunjukkan penurunan produksi NO secara signifikan, dengan inhibisi tertinggi mencapai 76.65% pada konsentrasi 25 µg/mL, hampir setara dengan inhibisi deksametason (80.67%). Temuan ini menguatkan potensi ekstrak kubis sebagai agen anti-inflamasi yang efektif untuk dermatitis kontak melalui mekanisme multi senyawa dan multi target.

Kata kunci: dermatitis, kubis, Brassicaceae, anti-inflamasi, *network pharmacology*, *molecular docking*, LC-HRMS, sel RAW 264.7.

ABSTRACT

Contact dermatitis is an inflammatory skin condition caused by exposure to irritants or allergens, affecting 15%-20% of the global population. Topical corticosteroids are the primary therapy for contact dermatitis. However, long-term use can lead to side effects such as skin thinning. Therefore, a safer alternative therapy is needed. Cabbage (*Brassica oleracea*) contains bioactive compounds such as sulforaphane and Indole-3-Carbinol, which possess anti-inflammatory and antioxidant activities. This study aims to identify the active compounds in cabbage, analyze their interactions with biological targets in inflammatory pathways through a network pharmacology approach, and evaluate their anti-inflammatory potential in dermatitis through molecular docking and measurement of NO production inhibition in LPS-stimulated RAW 264.7 cells using the Griess method to prove its effectiveness as an alternative therapy for contact dermatitis.

Secondary metabolite identification was performed using LC-HRMS. The spectrum data were analyzed using Compound Discoverer 3.3 software with mzCloud and ChemSpider databases. Network pharmacology studies were conducted using Cytoscape software with ClusterOne and CytoHubba plugins. Validation was carried out through molecular docking using AutoDock Vina, and *in vitro* testing on RAW 264.7 macrophage cells stimulated with LPS to measure Nitric Oxide (NO) levels using the Griess assay. *In vitro* test data were statistically analyzed using one-way ANOVA.

LC-HRMS analysis identified 119 secondary metabolite compounds, including Sulforaphane, Malyngic acid, Indole-3-Carbinol, Iberin, 2-hydroxy palmitic acid, C16 Sphinganine, 1-O-(2R-hydroxy-hexadecyl)-sn-glycerol, N-palmitoyl alanine, Stigmasta-3,5-diene, 1-palmitoylglycerol. Network pharmacology studies revealed that these compounds can interact with 13 inflammatory protein targets involved in signaling pathways related to contact dermatitis: TLR4, NFKB1, STAT3, BCL2, PTGS2, EGFR, HSP90AA1, MMP9, TLR2, PPARG, MAPK3, HMOX1, and NR3C1. Molecular docking showed binding energies of the compounds to MAPK3, PTGS2, and MMP9 ranging from -4.06 to -7.4 kcal/mol. *In vitro* tests on RAW 264.7 cells demonstrated a significant decrease in NO production, with the highest inhibition reaching 76.65% at a concentration of 25 µg/mL, nearly equivalent to Dexamethasone's inhibition (80.67%). These findings reinforce the potential of cabbage extract as an effective anti-inflammatory agent for contact dermatitis through a multi-compound and multi-target

Keywords: dermatitis, cabbage, Brassicaceae, anti-inflammatory, network pharmacology, molecular docking, LC-HRMS, RAW 264.7 cells.