

INTISARI

Diabetes neuropati merupakan gangguan saraf yang dapat terjadi pada penderita diabetes, yang dapat menyebabkan nyeri, kehilangan mobilitas fungsional, dan, dalam kasus yang parah, memerlukan amputasi. *Andrographis paniculata* (Burm.f.) Nees (AP) telah dilaporkan menurunkan kadar glukosa darah pada kondisi diabetes melitus, sementara *Zingiber officinale* Rosc (ZO) menunjukkan efek analgesik dan neuroprotektif. Penelitian ini bertujuan untuk mengevaluasi parameter standardisasi fraksi AP dan fraksi ZO. Selanjutnya, penelitian ini bertujuan untuk menyelidiki target protein dan jalur pensinyalan senyawa andrografolida dan 6-shogaol dalam mengatasi diabetes neuropati melalui analisis *Network Pharmacology* (NP).

Pada penelitian ini dilakukan evaluasi parameter standardisasi dan analisis NP. Evaluasi standardisasi meliputi analisis fitokimia kualitatif dan kuantitatif, organoleptik, kadar air, dan uji cemaran mikroba ALT dan AKK dari Fraksi Etil Asetat Sambiloto (FEAS) dan Fraksi Etil Asetat Jahe (FEAJ). NP dibuat dengan mengumpulkan data protein dari berbagai *database* yang terdiri dari data protein yang menjadi target senyawa dan data protein yang berhubungan dengan penyakit. Selanjutnya, data protein yang terkumpul dianalisis dengan melihat jaringan interaksi antar protein. Identifikasi target protein kunci dipilih berdasarkan nilai *degree* tertinggi dalam jaringan. Data jalur persinyalan dikumpulkan dari DAVID. Jalur persinyalan dengan *p-value* ≤ 0.01 dipilih secara berurutan. Analisis menggunakan SRplot untuk mengidentifikasi jalur persinyalan yang terlibat dalam penyakit diabetes neuropati.

FEAS dan FEAJ telah memenuhi parameter standardisasi, dengan kandungan andrografolid sebesar $14,01 \pm 0,61\%$ dan kandungan 6-shogaol sebesar $3,44 \pm 0,30\%$. Senyawa tunggal dan kombinasi senyawa andrografolid dan 6-shogaol menargetkan protein kunci, yaitu PIK3R1, PIK3CD, dan PIK3CB. Kombinasi andrografolid dan 6-shogaol menargetkan jalur pensinyalan di antaranya *Sphingolipid signaling pathway*, *AGE-RAGE signaling pathway in diabetic complications*, dan *Chemokine signaling pathway*. Hasil ini menunjukkan AP dan ZO berpotensi dikembangkan sebagai terapi herbal kombinasi untuk pengobatan neuropati diabetes.

Keywords: *Andrographis paniculata* (Burm.f.) Nees; *Zingiber officinale* Rosc.; Andrografolid, 6-shogaol; Standardisasi; *Network Pharmacology*

ABSTRACT

Diabetic neuropathy is nerve impairment that can occur in people with diabetes, which may cause pain, functional mobility loss, and, in severe cases, require amputation. *Andrographis paniculata* (Burm.f.) Nees has been reported to lower blood glucose in diabetes mellitus, while *Zingiber officinale* Rosc exhibits analgesic and neuroprotective effects. This study aimed to evaluate standardization parameters of the *Andrographis paniculata* (Burm.f.) Nees fraction and the *Zingiber officinale* Rosc fraction. Furthermore, it aimed to investigate the protein targets and signaling pathways of andrographolide and 6-shogaol compounds in addressing diabetic neuropathy through Network Pharmacology analysis.

This study involved the evaluation of standardization parameters and NP analysis. Standardization evaluation includes qualitative and quantitative phytochemical analysis, organoleptic, water content, and ALT and AKK microbial contamination tests from Sambiloto Ethyl Acetate Fraction (FEAS) and Ginger Ethyl Acetate Fraction (FEAJ). Protein data, including compound-targeted and disease-associated proteins, were collected from various databases for NP construction. Furthermore, the collected protein data were analyzed by examining the interaction protein network. Identification of key protein targets was selected based on the highest degree value in the network. Signaling pathway data were collected from DAVID. Signaling pathways with p-value ≤ 0.01 were selected. SRplot was utilized to identify signaling pathways involved in diabetic neuropathy.

FEAS and FEAJ have fulfilled standardization parameters, with andrographolide content at $14.01 \pm 0.61\%$ and 6-shogaol content at $3.44 \pm 0.30\%$. The single and combined compounds targeted key proteins, including PIK3R1, PIK3CD, and PIK3CB. The combination of andrographolide and 6-shogaol targeted the sphingolipid signaling pathway, the AGE-RAGE signaling pathway in diabetic complications, and the chemokine signaling pathway, all involved in developing diabetic neuropathy. These findings suggest that *Andrographis paniculata* and *Zingiber officinale* have the potential to be developed as a combination herbal therapy for the treatment of diabetic neuropathy.

Keywords: *Andrographis paniculata* (Burm.f) Nees; *Zingiber officinale* Rosc.;
Andrographolide, *6-shogaol*; *Standardization*; *Network Pharmacology*