ABSTRAK

Disfungsi ereksi merupakan gangguan fungsi seksual pada pria yang ditandai dengan ketidakmampuan mencapai atau mempertahankan ereksi yang cukup untuk melakukan hubungan seksual secara memuaskan. Meskipun inhibitor phosphodiesterase-5 (PDE5) masih menjadi terapi utama, penggunaannya memiliki keterbatasan berupa efek samping, kontraindikasi, dan respons terapi yang bervariasi. Oleh karena itu, pengembangan kandidat terapi alternatif berbasis bahan alam menjadi salah satu pendekatan yang menjanjikan. *Mikania cordata* (Burm.f.) B.L.Rob. merupakan tanaman obat yang kaya akan metabolit sekunder bioaktif dengan aktivitas antioksidan dan antiinflamasi, namun mekanisme molekulernya terhadap disfungsi ereksi belum banyak dikaji. Penelitian ini bertujuan mengkaji potensi *Mikania cordata* sebagai kandidat terapi disfungsi ereksi melalui pendekatan terintegrasi *network pharmacology* dan *molecular docking*. Penelitian dilakukan secara *in silico* dengan mengidentifikasi profil metabolit ekstrak etanol 96% *Mikania cordata* menggunakan LC-HRMS. Senyawa dominan dipilih melalui *Principal Component Analysis* (PCA) dan studi literatur, kemudian dievaluasi berdasarkan *Pa score*, *drug-likeness*, dan prediksi toksisitas menggunakan berbagai platform bioinformatika. Target protein diprediksi menggunakan SwissTargetPrediction dan TargetNet, kemudian diintegrasikan dengan gen terkait disfungsi ereksi melalui analisis *protein-protein interaction* dan pengayaan jalur KEGG. Target utama yang diperoleh meliputi PDE5A, AKT1, *endothelial nitric oxide synthase* (eNOS), *neuronal nitric oxide synthase* (nNOS), dan *inducible nitric oxide synthase* (iNOS). Hasil *molecular docking* menunjukkan beberapa senyawa bioaktif memiliki afinitas ikatan yang baik serta membentuk interaksi yang stabil dengan protein target. Analisis *network pharmacology* mengindikasikan keterlibatan senyawa dalam regulasi jalur PI3K-Akt, HIF-1, cGMP-PKG, dan *nitric oxide signaling* yang berperan dalam fungsi ereksi. Temuan ini menunjukkan bahwa *Mikania cordata* berpotensi sebagai kandidat terapi alami disfungsi ereksi dan memberikan dasar ilmiah untuk penelitian lanjutan secara *in vitro* maupun *in vivo*.

Kata kunci: *Mikania cordata*, disfungsi ereksi, *network pharmacology*, *molecular docking*, LC-HRMS, *in silico*.

ABSTRACT

Erectile dysfunction is a male sexual disorder characterized by the inability to achieve or sustain an erection adequate for satisfactory sexual performance. Although phosphodiesterase-5 (PDE5) inhibitors remain the primary therapeutic option, their clinical application is often restricted by adverse reactions, contraindications, and inconsistent treatment outcomes. Consequently, increasing attention has been directed toward identifying natural product-derived compounds as potential alternative therapeutic agents. *Mikania cordata* (Burm.f.) B.L.Rob. is a medicinal plant recognized for its abundance of bioactive secondary metabolites exhibiting antioxidant and anti-inflammatory activities. Nevertheless, the molecular basis underlying its potential role in the management of erectile dysfunction has not yet been comprehensively elucidated. This study was designed to investigate the potential of *Mikania cordata* as a source of candidate compounds for erectile dysfunction therapy by integrating network pharmacology with molecular docking techniques. An *in silico* analysis was performed by profiling metabolites from a 96% methanolic extract of *Mikania cordata* using liquid chromatography–high resolution mass spectrometry (LC-HRMS). Dominant metabolites were selected through Principal Component Analysis (PCA) and literature screening, followed by prediction of biological activity (Pa score), drug-likeness, and toxicity using multiple bioinformatics platforms. Potential protein targets were identified using SwissTargetPrediction and TargetNet and subsequently integrated with erectile dysfunction-associated genes through protein-protein interaction and KEGG pathway analyses. The principal targets included PDE5A, AKT1, endothelial nitric oxide synthase (eNOS), neuronal nitric oxide synthase (nNOS), and inducible nitric oxide synthase (iNOS). Molecular docking demonstrated favorable binding affinities and stable interactions between several bioactive compounds and the target proteins. Furthermore, network pharmacology revealed that these compounds may influence the PI3K-Akt, HIF-1, cGMP-PKG, and nitric oxide signaling pathways, all of which are closely associated with the regulation of erectile function. Overall, the findings suggest that *Mikania cordata* possesses considerable potential as a natural therapeutic candidate for erectile dysfunction and provide a scientific foundation for subsequent experimental validation through *in vitro* and *in vivo* studies.

Keywords: *Mikania cordata*, erectile dysfunction, network pharmacology, molecular docking, LC-HRMS, *in silico*.