

INTISARI

Diabetes Melitus Tipe 2 (DMT2) merupakan gangguan metabolisme kronis dengan prevalensi global yang terus meningkat, ditandai oleh resistensi insulin dan peningkatan kadar glukosa darah. Pengelolaan glikemik pada DMT2 sering kali sulit dicapai menggunakan terapi konvensional karena kompleksitas kondisi ini, sehingga diperlukan alternatif yang aman dan efektif. Daun salam (*Syzygium polyanthum* Wight.), yang telah dimanfaatkan secara tradisional di Indonesia sebagai agen antidiabetes, mengandung senyawa metabolit sekunder seperti flavonoid dan fenolik yang berpotensi memberikan efek terapeutik dengan risiko efek samping rendah. Penelitian ini bertujuan untuk mengevaluasi potensi antidiabetes daun salam melalui analisis fitokimia, uji aktivitas antioksidan, *network pharmacology*, dan *molecular docking* guna mengidentifikasi senyawa aktif, jalur aksi, serta mekanisme terapeutiknya dalam pengelolaan DMT2.

Metode penelitian meliputi ekstraksi dan fraksinasi daun salam menggunakan pelarut etil asetat, n-heksan, dan air untuk mengukur kandungan total flavonoid, total fenolik, serta aktivitas antioksidan dengan metode penangkapan radikal 2,2-diphenyl-1-picrylhydrazyl (DPPH). Analisis *liquid chromatography-high resolution mass spectrometry* (LC-HRMS) dilakukan untuk mengidentifikasi senyawa kimia, diikuti oleh *network pharmacology* untuk menyaring senyawa aktif dan protein target utama yang berperan dalam jalur biologis. *Molecular docking* diterapkan untuk mengevaluasi afinitas ikatan senyawa aktif terhadap protein target. Data dianalisis secara kuantitatif untuk menentukan nilai IC₅₀ aktivitas antioksidan, kadar senyawa bioaktif, serta skor afinitas dari simulasi docking, dengan fokus pada jalur sinyal seperti *insulin resistance*, PI3K-Akt, dan *FoxO signaling*.

Fraksi etil asetat memiliki aktivitas antioksidan paling tinggi dengan nilai IC₅₀ 41,71 µg/ml, serta kandungan flavonoid (198,20 mgGAE/g) dan fenolik (62,06 mgQE/g) yang signifikan. Analisis LC-HRMS mengidentifikasi 424 senyawa dengan 10 senyawa aktif terpilih, termasuk asam 6-formilsalisilat dan braktein. *Network pharmacology* menunjukkan protein kunci AKT1 dan PPAR Gamma yang berperan dalam jalur *insulin resistance*, PI3K-Akt, dan *FoxO signaling*. *Molecular docking* mengindikasikan afinitas ikatan asam 6-formilsalisilat dengan AKT1 (-8,91) dan braktein dengan PPAR Gamma (-7,49). Fraksi etil asetat daun salam menunjukkan potensi antidiabetes melalui aktivitas antioksidan yang kuat dan senyawa aktif yang mendukung pengelolaan DMT2 melalui jalur sinyal insulin.

Kata kunci: Daun salam, diabetes melitus tipe 2, *network pharmacology* dan *molecular docking*

ABSTRACT

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder with increasing global prevalence, characterized by insulin resistance and elevated blood glucose levels. Glycemic management in T2DM is often difficult to achieve using conventional therapies due to the complexity of this condition, so safe and effective alternatives are needed. Bay leaf (*Syzygium polyanthum* Wight.), which has been traditionally utilized in Indonesia as an antidiabetic agent, contains secondary metabolite compounds such as flavonoids and phenolics that have the potential to provide therapeutic effects with low risk of side effects. This study aims to evaluate the antidiabetic potential of bay leaves through phytochemical analysis, antioxidant activity test, network pharmacology, and molecular docking to identify active compounds, pathways of action, and therapeutic mechanisms in the management of T2DM

The research methods included extraction and fractionation of bay leaves using ethyl acetate, n-hexane, and water solvents to measure total flavonoid content, total phenolic content, and antioxidant activity using 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging method. Liquid chromatography-high resolution mass spectrometry (LC-HRMS) analysis was performed to identify chemical compounds, followed by network pharmacology to screen active compounds and key target proteins involved in biological pathways. Molecular docking was applied to evaluate the binding affinity of active compounds to target proteins. Data were quantitatively analyzed to determine the IC₅₀ value of antioxidant activity, bioactive compound content, as well as affinity scores from docking simulations, focusing on signaling pathways such as insulin resistance, PI3K-Akt, and FoxO signaling.

The ethyl acetate fraction had the highest antioxidant activity with an IC₅₀ value of 41.71 µg/ml, and significant flavonoid (198.20 mgGAE/g) and phenolic (62.06 mgQE/g) contents. LC-HRMS analysis identified 424 compounds with 10 active compounds selected, including 6-formylsalicylic acid and bractein. Network pharmacology showed key proteins AKT1 and PPAR Gamma that play a role in insulin resistance, PI3K-Akt, and FoxO signaling pathways. Molecular docking indicated the binding affinity of 6-formylsalicylic acid with AKT1 (-8.91) and bractein with PPAR Gamma (-7.49). The ethyl acetate fraction of bay leaves shows antidiabetic potential through strong antioxidant activity and active compounds that support the management of T2DM through the insulin signaling pathway.

Keywords: Bay leaf, type 2 diabetes mellitus, network pharmacology and molecular docking.