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**Aktivitas Penghambatan Enzim Dipeptidyl Peptidase-IV (DPP-Iv) dari Ekstrak Daun Kratom (Mitragyna
Speciosa Korth) dan Identifikasi Kandungan Kimianya**
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INTISARI

Diabetes melitus tipe 2 merupakan penyakit metabolik yang memerlukan pengembangan terapi alternatif berbasis bahan alam. Salah satu pendekatan yang potensial adalah penghambatan enzim dipeptidyl peptidase-IV (DPP-IV), yang berperan dalam degradasi hormon inkretin. Daun kratom (*Mitragyna speciosa*) diketahui mengandung alkaloid indol yang berpotensi menjadi senyawa bioaktif untuk diabetes. Penelitian ini bertujuan untuk mengevaluasi pengaruh variasi pelarut ekstraksi terhadap karakteristik kimia ekstrak daun kratom, hubungannya dengan aktivitas penghambatan enzim DPP-IV secara *in vitro*, serta mengidentifikasi kandungan senyawa pada ekstrak yang paling aktif.

Ekstraksi dilakukan menggunakan air dan etanol dengan konsentrasi 30%, 50%, 70%, dan 90%. Karakterisasi meliputi penentuan rendemen, identifikasi alkaloid secara kualitatif menggunakan kromatografi lapis tipis (KLT), serta penetapan kadar alkaloid total dengan metode bromocresol green menggunakan yohimbine sebagai standar. Aktivitas penghambatan DPP-IV diuji secara *in vitro*, kemudian dilanjutkan dengan penentuan nilai IC_{50} pada ekstrak yang paling aktif. Hubungan kadar alkaloid total dengan aktivitas inhibisi dianalisis menggunakan korelasi Spearman dan regresi linier, sedangkan profil metabolit ditentukan menggunakan LC-HRMS.

Hasil penelitian menunjukkan bahwa ekstrak etanol 30% menghasilkan rendemen tertinggi (27,39%), sedangkan ekstrak etanol 90% memiliki kadar alkaloid total tertinggi (141,53 ± 2,44 mg/g ekstrak), aktivitas penghambatan DPP-IV sebesar 72,87 ± 0,30%, serta nilai IC_{50} sebesar 172 µg/mL. Kadar alkaloid total berkorelasi positif sangat kuat dengan aktivitas inhibisi DPP-IV (r_s = 0,896; $p < 0,001$; R^2 = 0,85). Analisis LC-HRMS mendeteksi 381 senyawa, dengan 15 senyawa teridentifikasi terbaik yang didominasi oleh *mitragynine* dan *7-hydroxymitragynine*. Hasil ini menunjukkan bahwa ekstrak etanol 90% daun kratom berpotensi menjadi kandidat inhibitor DPP-IV alami untuk pengembangan fitofarmaka antidiabetes.

Kata Kunci: Alkaloid Total, Antidiabetes, DPP-IV, LC-HRMS, *Mitragyna speciosa*, *mitragynine*

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ABSTRACT

Type 2 diabetes mellitus is a metabolic disorder that requires the development of alternative therapies derived from natural products. One promising therapeutic approach is the inhibition of the enzyme dipeptidyl peptidase-IV (DPP-IV), which plays a crucial role in the degradation of incretin hormones. *Mitragyna speciosa* leaves contain indole alkaloids with potential antidiabetic activity. This study aimed to evaluate the effects of different extraction solvents on the chemical characteristics of *Mitragyna speciosa* leaf extracts, investigate the relationship between these characteristics and in vitro DPP-IV inhibitory activity, and identify the chemical constituents of the most active extract.

Extraction was performed using water and ethanol at concentrations of 30%, 50%, 70%, and 90%. The extraction characterisation included determination of extraction yield, qualitative alkaloid identification by thin-layer chromatography (TLC), and determination of total alkaloid content using the bromocresol green (BCG) method with yohimbine as the calibration standard. DPP-IV inhibitory activity was evaluated in vitro, followed by determination of the IC_{50} value of the most active extract. The relationship between total alkaloid content and DPP-IV inhibitory activity was analysed using Spearman's correlation and linear regression. At the same time, metabolite profiling was performed using liquid chromatography–high-resolution mass spectrometry (LC–HRMS).

The results showed that the 30% ethanol extract produced the highest extraction yield (27.39%). In contrast, the 90% ethanol extract exhibited the highest total alkaloid content (141.53 ± 2.44 mg/g extract), the strongest DPP-IV inhibitory activity (72.87 ± 0.30%), and an IC_{50} value of 172 µg/mL. Total alkaloid content showed a very strong positive correlation with DPP-IV inhibitory activity (r_s = 0.896, $p < 0.001$; $R^2 = 0.85$). LC–HRMS analysis detected 381 compounds, of which 15 were tentatively identified, with *mitragynine* and *7-hydroxymitragynine* being the predominant constituents. These findings suggest that the 90% ethanol extract of *Mitragyna speciosa* leaves has promising potential as a natural DPP-IV inhibitor for the development of antidiabetic phytopharmaceuticals.

Keywords: *Antidiabetic Activity, total alkaloid content, DPP-IV, LC-HRMS, Mitragyna speciosa, mitragynine*