

INTISARI

Diabetes melitus tipe 2 (DM tipe 2) merupakan gangguan metabolik akibat kerusakan sel- β -pankreas dan penurunan sensitivitas jaringan terhadap insulin. Prevalensi DM tipe 2 terus meningkat secara global, sehingga diperlukan pengembangan alternatif terapi berbasis herbal. Daun juwet (*Syzygium cumini* L.) secara empiris digunakan untuk mengatasi diabetes, namun diperlukan optimasi metode ekstraksi untuk memperoleh ekstrak dengan kandungan senyawa bioaktif yang lebih efektif. Penelitian ini bertujuan mengoptimasi produksi ekstrak daun *S. cumini* berbasis ekstraksi berbantu ultrasonik (*Ultrasound-Assisted Extraction*, UAE) sehingga dihasilkan ekstrak kaya polifenol dengan potensi antidiabetes.

Penelitian dilaksanakan dalam tiga tahap: (1) optimasi kondisi UAE menggunakan metode *Response Surface Methodology-Box Behnken Design* (RSM-BBD) dengan parameter rendemen, kadar flavonoid total (TFC), kadar fenolik total (TPC), serta aktivitas penghambatan enzim *dipeptidil-peptidase IV* (DPP-IV); (2) fraksinasi ekstrak optimal menggunakan pelarut bertingkat (*n*-heksan, kloroform, etil asetat, dan air); (3) uji *in vivo* aktivitas antidiabetes pada tikus model DM tipe 2 neonatal streptozotosin, meliputi parameter glukosa darah, insulin, *Glucagon Like Peptide-1* (GLP-1), aktivitas enzim superoksida dismutase (SOD), HOMA-IR, HOMA- β , serta analisis histopatologi dan imunohistokimia pankreas.

Hasil penelitian menunjukkan kondisi optimum UAE (perbandingan pelarut-bahan 21 mL/g; konsentrasi etanol 70%; suhu 20 °C; waktu 30 menit) menghasilkan perolehan ekstrak 82,05% b/b, TFC 3,34 mg QE/g pada konsentrasi ekstrak 10000 ppm, TPC 66,56 mkg GAE/g pada konsentrasi ekstrak 1000 ppm, dan aktivitas penghambatan DPP-IV 68,38% pada konsentrasi 1300 ppm. Fraksi etil asetat merupakan fraksi terbaik dengan kandungan polifenol tinggi dan aktivitas penghambatan DPP-IV sebesar 53,79% dengan konsentrasi sama dengan ekstrak etanol. Ekstrak etanol dan fraksi etil asetat mengandung senyawa *Myricitrin*, *7-Hydroxyflavan*, *5,6-dimethoxy-2-(2-methoxyphenyl)-4H-chromen-4-one*, *Gallic acid*, *3,5-Dihydroxy-4-isopropyl-trans-stilbene* dengan LC-HRMS. Uji *in vivo* menunjukkan ekstrak etanol maupun fraksi etil asetat dosis 400 mg/kg BB menurunkan kadar glukosa darah, meningkatkan insulin dan GLP-1, meningkatkan aktivitas enzim SOD, serta memperbaiki ekspresi insulin pada *insula Langerhans*. Dengan demikian, ekstrak etanol dan fraksi etil asetat daun *S. cumini* berpotensi dikembangkan lebih lanjut sebagai kandidat bahan baku herbal antidiabetes tipe 2.

Kata Kunci: *Syzygium cumini*, Ekstraksi berbantu ultrasonik, DPP-IV, Polifenol, Diabetes Mellitus tipe 2

ABSTRACT

Type 2 diabetes mellitus (type 2 DM) is a metabolic disorder caused by damage to pancreatic β -cells and decreased tissue insulin sensitivity. The prevalence of type 2 DM continues to increase globally, necessitating the development of alternative herbal-based therapies. Java plum leaves (*Syzygium cumini* L.) have been empirically used to treat diabetes, but optimization of extraction methods is necessary to obtain extracts with more effective bioactive compounds. This study aimed to optimize the production of extract from *S. cumini* leaves using ultrasound-assisted extraction (UAE) to produce a polyphenol-rich fraction with antidiabetic potential.

The study was conducted in three stages: (1) optimization of UAE conditions using the Response Surface Methodology–Box Behnken Design (RSM-BBD) method, with parameters such as yield, total flavonoid content (TFC), total phenolic content (TPC), and dipeptidyl-peptidase IV (DPP-IV) inhibitory activity. (2) optimal extract fractionation using graded solvents (n-hexane, chloroform, ethyl acetate, and water); (3) in vivo test of antidiabetic activity in neonatal streptozotocin type 2 DM model rats, including blood glucose parameters, insulin, Glucagon Like Peptide-1 (GLP-1), superoxide dismutase (SOD) enzyme activity, HOMA-IR, HOMA- β , as well as histopathological and immunohistochemical analysis of the pancreas.

The research results show that the optimal UAE conditions (solvent-to-material ratio 21 mL/g; ethanol concentration 70%; temperature 20°C; time 30 minutes) yield an extract recovery of 82,05% w/w, total flavonoids of 3,34 mg QE/g at an extract concentration of 10000 ppm, total phenolics of 66.56 μ g GAE/g at an extract concentration of 1000 ppm, and DPP-IV inhibitory activity of 68,38% at a concentration of 1300 ppm. The ethyl acetate fraction is the best fraction, with a high polyphenol content and DPP-IV inhibitory activity of 53,79% at the same concentration as the ethanol extract. The ethanol extract and ethyl acetate fraction contain the compounds myricitrin, 7-hydroxyflavan, 5,6-dimethoxy-2-(2-methoxyphenyl)-4H-chromen-4-one, gallic acid, and 3,5-dihydroxy-4-isopropyl-trans-stilbene, as determined by LC-HRMS. In vivo tests showed that both the ethanol extract and the ethyl acetate fraction at a dose of 400 mg/kg body weight reduced blood glucose levels, increased insulin and GLP-1, enhanced SOD enzyme activity, and improved insulin expression in the islets of Langerhans. Thus, the ethanol extract and ethyl acetate fraction of *S. cumini* leaves have the potential for further development as a candidate for raw herbal materials against type 2 diabetes.

Keywords: *Syzygium cumini*, ultrasonic-assisted extraction, DPP-IV, polyphenols, type 2 diabetes mellitus