ABSTRAK

Pendahuluan: Diabetes melitus (DM) merupakan gangguan metabolik yang ditandai dengan hiperglikemia, sering dikaitkan dengan obesitas, dislipidemia, hipertensi, dan penyakit kardiovaskular, terutama pada DM tipe 2. Gaya hidup sedentari dan obesitas menjadi faktor risiko yang dapat dimodifikasi. Di Indonesia, penggunaan obat tradisional untuk DM lebih diminati karena dinilai lebih aman dan ekonomis dibandingkan obat sintetis. **Metode:** Penelitian ini menggunakan desain eksperimental *randomized post-test only control group* dengan 25 ekor tikus Wistar jantan yang dibagi dalam lima kelompok: normal, aloksan dan diet tinggi lemak, pioglitazone, ekstrak tanaman, serta kombinasi pioglitazone dan ekstrak. Induksi obesitas dilakukan dengan pemberian diet tinggi lemak selama 27 hari, diikuti pemberian aloksan dosis 100 mg/KgBB untuk meningkatkan kadar glukosa darah. Pengukuran kadar glukosa dilakukan pada hari ke-4 dan ke-14, HbA1c pada hari ke-26, serta analisis histopatologi pankreas setelah terminasi. **Hasil:** Uji *Kruskal-Wallis* menunjukkan perbedaan signifikan pada peningkatan berat badan ($p = 0,016$) dan kadar glukosa darah ($p = 0,003$) antar kelompok. Meski tidak ada perbedaan signifikan penurunan kadar glukosa darah antar kelompok pada uji *Mann-Whitney* ($p = 0,05$), kelompok 5 mengalami penurunan terbesar. Uji *one way ANOVA* menunjukkan kombinasi ekstrak dan pioglitazone secara signifikan menurunkan HbA1c ($p < 0,001$). Uji *post hoc Tukey LSD* menunjukkan kelompok 2 memiliki HbA1c tertinggi, sedangkan kelompok 4 menunjukkan penurunan paling baik. Secara histopatologi, kelompok yang menerima pioglitazone dan ekstrak menunjukkan kerusakan pada pulau Langerhans. **Kesimpulan:** Kombinasi ekstrak ikan gabus, meniran, temulawak, serta pioglitazone efektif menurunkan kadar glukosa darah dan HbA1c. Tetapi tidak memperbaiki kerusakan histopatologi pulau Langerhans. Stres oksidatif dari piogliatazone, dosis ekstrak serta aloksan diduga mempengaruhi hasil ini.

Kata kunci : Diabetes Melitus, Kombinasi ekstrak ikan gabus *(Channa striata)*, meniran *(Phyllanthus niruri* L.*)* dan temulawak *(Curcuma xanthorrhiza)*, Kadar Glukosa Darah, HbA1c, Histopatologi pankreas

ABSTRACT

Introduction*: Diabetes mellitus (DM) is a metabolic disease characterized by high blood sugar levels, known as hyperglycemia. Obesity, dyslipidemia, hypertension, and cardiovascular disease are common complications of DM, especially in type 2 diabetics. A sedentary lifestyle and obesity are modifiable risk factors. In Indonesia, traditional medicine is more commonly utilized for the treatment of diabetic mellitus (DM) since it is perceived as a safer and more cost-effective option than synthetic medications.* ***Method:*** *This study employed a randomized post-test only control group experimental design with 25 male Wistar rats, which were divided into five groups: a control group, a group that received alloxan and a high-fat diet, a group that received pioglitazone, a group that received a plant extract, and a group that received a combination of pioglitazone and the plant extract. The induction of obesity was achieved through a high-fat diet for 27 days, followed by the administration of alloxan at a dose of 100 mg/kg body weight (BW), which was employed to elevate blood glucose levels. Glucose levels were measured on days 4 and 14, HbA1c on day 26, and pancreatic histopathology was analyzed after termination.* ***Results:*** *The Kruskal-Wallis test revealed statistically significant differences in weight gain ($p = 0.016$) and blood glucose levels ($p = 0.003$). Although no significant difference in the reduction of blood glucose levels was observed between groups in the Mann-Whitney test ($p = 0.05$), group 5 demonstrated the most pronounced reduction. The one-way ANOVA test demonstrated that combining the extract and pioglitazone resulted in a statistically significant reduction in HbA1c ($p < 0.001$). The Tukey LSD post hoc test revealed that Group 2 exhibited the highest HbA1c levels, while Group 4 demonstrated the most pronounced reduction. The groups that received pioglitazone and the extract showed histopathological damage to the islets of Langerhans.*

Conclusion: *combining snakehead fish extract, meniran, temulawak, and pioglitazone is a practical approach for reducing blood glucose and HbA1c levels. However, this combination has not been observed to improve the*

histopathological damage to the islets of Langerhans. It is postulated that the influence of oxidative stress from pioglitazone, the extract dose, and alloxan may contribute to these observed results.

Keywords: *Diabetes mellitus, the combination of extracts of snakehead fish (Channa striata), meniran (Phyllanthus niruri L.), and temulawak (Curcuma xanthorrhiza), blood glucose levels, HbA1c, pancreatic histopathology*