Trop J Nat Prod Res, September 2025; 9(9): 4155 - 4161 **ISSN 2616-0684 (Print)**
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Original Research Article

Evaluation of the Antidiabetic Efficacy of Indigenous Indonesian Ethnomedicinal Herbal Infusions in a Streptozotocin-induced Diabetic Mouse Model

Mally G. Sholih[1], Munir A. Mulki[1]*, Marsah R. Utami[1]

[1]*Department of Pharmacy, Faculty of Health Sciences, Universitas Singaperbangsa Karawang, Karawang Regency, West Java, Indonesia*

ARTICLE INFO

Article history:
Received 06 June 2025
Revised 29 August 2025
Accepted 02 September
Published online 01 October 2025

ABSTRACT

Indonesia is abundant in natural resources, with approximately 35,000 species of higher plants, many known for medicinal properties. This study evaluated the antidiabetic effects of two herbal infusions in male Balb/c mice induced diabetes with streptozotocin (150 mg/kgBW intraperitoneally). The first infusion consisted of *Syzygium polyanthum* (bay leaves), *Andrographis paniculata* (sambiloto), and *Tinospora crispa* (brotowali stems), while the second was made from *Syzygium cumini* (jamblang bark). A pre- and post-test control group design was used following ethical approval. The mice were divided into five groups: positive control (metformin 65 mg/kgBW), negative control (physiological NaCl), and three test groups receiving herbal infusions at specific doses. Treatments were administered orally once daily for 21 consecutive days. Blood glucose levels were measured initially (day 0) and subsequently on days 7, 14, and 21 after 12-hour fasting periods. Infusions of *Syzygium polyanthum*, *Andrographis paniculata*, and *Tinospora crispa* was administered at doses of 1.95 g/20 gBW, 3.9 g/20 gBW, and 7.8 g/20 gBW, significantly reduced blood glucose levels compared to the negative control ($p < 0.05$). Similarly, *Syzygium cumini* bark infusions was administered at doses of 1.47 g/20 gBW, 1.76 g/20 gBW, and 2.06 g/20 gBW, also demonstrated significant reductions ($p < 0.05$). These findings suggest that the herbal infusions are effective in reducing blood glucose levels in streptozotocin-induced diabetic mice and have potential as natural antidiabetic agents, demonstrating both efficacy and statistical significance.

Keywords: Diabetes Mellitus, Blood Glucose Reduction, Streptozotocin, Herbal Infusion, Ethnomedicine, Antidiabetic Activity.

Introduction

Type 2 diabetes mellitus (T2DM) is a progressive disease characterised by the decline of pancreatic *β*-cell function, leading to reduced insulin secretion and decreased tissue sensitivity to insulin.[1] This condition results in disrupted carbohydrate, fat, and protein metabolism.[2] The International Diabetes Federation (IDF) estimates that the global prevalence of diabetes mellitus (DM) will increase from 537 million cases in 2021 to 783 million cases by 2045.[3] Meanwhile, the latest projections indicate that the prevalence of diabetes in Indonesia is estimated to increase from 9.19% (18.69 million cases) in 2020 to 16.09% (40.7 million) in 2045.[4] Lifestyle and dietary changes remain significant barriers to achieving effective T2DM management. Failure of oral diabetes medication often leads to complications associated with increased HbA1C levels exceeding 7%. T2DM treatment is typically a lifelong process. Insulin therapy, while effective for both type 1 and type 2 diabetes under certain conditions, is expensive and may cause side effects such as hypoglycaemia and allergic reactions. Most patients with T2DM are treated with metformin as the first-line therapy, while others may require combination therapy with additional antidiabetic medications.[4]

*Corresponding author. Email: munir.alinu@fikes.unsika.ac.id
Tel: +62 821 2878 7240

Citation: Mally G Sholih, Munir A Mulki, Marsah R Utami. Evaluation of the Antidiabetic Efficacy of Indigenous Indonesian Ethnomedicinal Herbal Infusions in a Streptozotocin-induced Diabetic Mouse Model. Trop J Nat Prod Res. 2025; 9(9) 4155 – 4161 https://doi.org/10.26538/tjnpr/v9i9.12

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria

However, prolonged use of synthetic drugs, including metformin, can lead to side effects such as gastrointestinal disturbances, lactic acidosis, vitamin B12 deficiency, and contraindications in patients with kidney and liver disorders, acidosis, hypoxia, or dehydration.[5] This has created a need for alternative therapies, including the use of traditional herbal medicine derived from plants.[6] Several medicinal plants have been used traditionally for diabetes management, including bay leaves (*Syzygium polyanthum*), bitter herb (*Andrographis paniculata* Ness), and brotowali (*Tinospora crispa* L.). Bay leaves are widely used in traditional medicine across Indonesia, particularly by the Balocci Baru community, for managing diabetes mellitus. Bay leaves contain flavonoids, saponins, tannins, and essential oils. Flavonoids are known to prevent degenerative diseases related to oxidative stress by protecting Langerhans cells in the pancreas.[7] Additionally, tannins in bay leaves can reduce blood glucose levels.[8] Previous studies have shown that bay leaf infusions effectively reduce blood glucose levels in male mice induced with oral glucose.[9] *Andrographis paniculata* contains andrographolide, an active compound with significant antidiabetic potential. It improves glucose metabolism and restores metabolic balance, particularly in diabetic-obese rat models, highlighting its promise as a natural therapeutic agent for diabetes management.[10] Meanwhile, in Thailand, *Tinospora crispa* (L.) is used traditionally as an antipyretic, antidiabetic, anti-inflammatory, and antimalarial.[11] Extracts of *Tinospora crispa* stems have been reported to reduce blood glucose levels more effectively than metformin.[12] An infusion comprising 50 g of bay leaves (*Syzygium polyanthum*), 50 g of bitter herb (*Andrographis paniculata* Ness), and 50 g of brotowali stems (*Tinospora crispa* L.) is used traditionally by the Sasak ethnic group in Mataram, Indonesia, for lowering blood glucose levels. This infusion is prepared by cleaning, drying, and grinding the ingredients into powder, which is then brewed with hot water. The preparation is consumed three times daily and forms part of Indonesia's ethnomedical practices.[13]
Another medicinal plant used for diabetes management is *Syzygium cumini* (jamblang). Among the Tidore ethnic group in Tidore Regency, a traditional infusion is prepared by boiling a piece of jamblang bark,

approximately palm-sized, in five cups of water until reduced to three cups. This infusion is consumed three times daily and represents the ethnopharmacological practices of Indonesia in addressing diabetes through natural remedies.[13] The jamblang bark contains active compounds such as betulinic acid, friedelin, epifriedelanol, eugenin, quercetin, kaempferol, myricetin, gallic acid, ellagic acid, bergenin, flavonoids, polyphenols, acetyl oleanolic acid, triterpenoid saponins, anthocyanins, and tannins. The primary antihyperglycaemic agents include flavonoids, tannins, and triterpenoid saponins.[14] Flavonoids and tannins are water-soluble, whereas triterpenoid saponins are hydrophobic.[15] Ethanol extracts of jamblang bark have shown antidiabetic efficacy in alloxan-induced diabetic rats.[16] Effective reductions in blood glucose levels have also been demonstrated with jamblang bark extracts at doses of 250 mg/kg body weight.[17]

Although the antidiabetic potential of jamblang bark ethanol extracts has been widely studied, limited research exists on its use as an infusion. The infusion method offers practical advantages, including ease of use, affordability, and alignment with traditional preparation methods used in Indonesian communities.[13]

This study addressed the knowledge gap by evaluating the antidiabetic efficacy of herbal infusions derived from Indonesian ethnomedicinal plants, specifically the infusion of jamblang bark (*Syzygium cumini*) and a herbal infusion composed of bay leaves (*Syzygium polyanthum*), sambiloto herb (*Andrographis paniculata* Ness), and brotowali stems (*Tinospora crispa* L.). By employing a practical infusion method, the research aligns with traditional medicine preparation techniques commonly used by local communities. This approach not only provides a simpler and more accessible alternative for diabetes treatment but also strengthens the scientific evidence for the global application of ethnomedicinal practices. Through its focus on culturally relevant, cost-effective treatments, this study contributes to the development of sustainable healthcare solutions for global diabetes management.

Materials and Methods

This experimental study employed a pre- and post-test control group design with multiple stages: obtaining ethical clearance from Universitas Yayasan Pendidikan Imam Bonjol (YPIB) Cirebon (Ethical Approval Numbers 054/KEPK/EC/I/2024 and 055/KEPK/EC/I/2024), plant identification and authentication, simplicia characterisation, herbal formulation preparation, phytochemical screening, animal preparation, test solution preparation, and evaluation of the antidiabetic activity of herbal infusions, including bay leaves (*Syzygium polyanthum*), bitter herb (*Andrographis paniculata* Ness), brotowali stems (*Tinospora crispa* L.), and jamblang bark (*Syzygium cumini*).

Materials

The equipment used included a digital analytical balance (OHAUS®), an oven (Memmert®), an oral syringe (Terumo®), blood glucose strips (Autocheck®), a glucometer (Autocheck®), a portable stove (GSF®), and a thermometer (TP 101®). Materials used were bay leaves, brotowali stems, bitter herb, metformin, Na-CMC, honey, distilled water, alloxan, hydrochloric acid, Mayer's reagent, Bouchardat's reagent, Dragendorff's reagent, ammonia, chloroform, ethanol, hot water, ferric chloride 5% solution, and Liebermann-Burchard reagent.

Plant Collection and Identification:

All plant materials used in this study were collected on March 22, 2024, from the Balittro Research Center in Bogor, Indonesia (Research Center for Spices and Medicinal Plants) (coordinates: -6.576845, 106.786364). The collected plant species consisted of bay leaf (*Syzygium polyanthum* (Wight) Walp.), sambiloto (*Andrographis paniculata* (Burm.f.) Wall. ex Nees), brotowali (*Tinospora crispa* (L.) Hook.f. & Thomson), and jamblang (*Syzygium cumini* (L.) Skeels). The plant parts utilized included leaves of *S. polyanthum*, the whole herb of *A. paniculata*, stems of *T. crispa*, and stem bark of *S. cumini*. Taxonomic identification of all collected plant specimens was conducted at the Herbarium Jatinangoriense, Biosystematics and Molecular Laboratory, Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Padjadjaran, Bandung, Indonesia. The voucher specimens were authenticated and deposited at the same herbarium for future reference, with voucher numbers 358 for *S. polyanthum*, 359 for *A. paniculata*, 360 for *T. crispa*, and 351 for *S. cumini*.

Preparation of Streptozotocin (STZ) Solution

STZ was used to induce diabetes at a dose of 150 mg/kgBW for male mice weighing 20 g, corresponding to 3 mg/20gBW. The required STZ was weighed and dissolved in physiological NaCl. The was administered intraperitoneally.

Preparation of Metformin Solution

The commonly used metformin dose is 500 mg, and the mouse-human dose conversion factor is 0.0026. Therefore, for a 20 g mouse, the required dose was 1.3 mg/20 gBW. The metformin solution was prepared by grinding the tablet, weighing the required dose, and dissolving it in physiological NaCl to 100 mL.

Preparation of Bay Leaf, Bitter Herb, and Brotowali Stem Infusion

The infusion was prepared by mixing dried simplicia of bay leaves (*Syzygium polyanthum*), bitter herb (*Andrographis paniculata* Ness), and brotowali stems (*Tinospora crispa* L.) in a ratio of 1:1:1 (w/w), with each ingredient weighed at 156 grams. This mixture (totaling 468 grams) was then dissolved in 300 mL of distilled water and heated at 95°C for 15 minutes. After heating, the infusion was filtered through filter paper and allowed to cool. The final infusion was administered orally at doses of 1.95 g/20 gBW, 3.9 g/20 gBW, and 7.8 g/20 gBW once daily according to the experimental groups.

Preparation of Jamblang Bark Infusion

The infusion of jamblang bark (*Syzygium cumini*) was prepared by boiling 618 g of dried bark simplicia in 300 mL of distilled water at 95°C for 15 minutes. After boiling, the infusion was filtered through filter paper and allowed to cool before use. The final infusion was administered orally at doses of 1.47 g/20 gBW, 1.76 g/20 gBW, and 2.06 g/20 gBW once daily according to the respective experimental groups.

Animal Preparation

Male mice, strain Balb/c, aged 3-4 months and weighing 20-25 g, were used. A total of 25 mice were divided into five groups, each consisting of five mice. Before treatment, the mice were acclimatised for seven days.

Preliminary Testing

The mice were induced diabetes with STZ intraperitoneally on the seventh day after acclimatisation. After three days, fasting blood glucose levels were measured using a glucometer. Before measurement, the mice were fasted from food but allowed to drink water for 8–12 hours. After determining the glucose levels, the mice were treated according to their respective groups for 21 days. The positive control group received metformin, and the negative control group was administered only physiological NaCl, and the three test groups received the herbal infusions.

Antidiabetic Testing

The test animals were divided into eight groups: the positive control group (metformin 1.3 mg/20 gBW), the negative control group receiving physiological NaCl, three test groups for the bay leaf-bitter herb-brotowali stem infusion at doses of 1.95 g/20 gBW, 3.9 g/20 gBW, and 7.8 g/20 gBW, and three test groups for the jamblang bark infusion at doses of 1.47 g/20 gBW, 1.76 g/20 gBW, and 2.06 g/20 gBW. Blood glucose levels were measured five times throughout the experiment: initially post-acclimatization to determine baseline glucose levels for inclusion criteria, followed by measurements on days 0, 7, 14, and 21 to assess fasting glucose levels after 12-hour fasting periods. Blood samples for glucose measurements were collected from tail cuts approximately 0.2–2 cm in length using blood glucose strips (Autocheck®) and a glucometer (Autocheck®).

Data Analysis

Data normality was assessed to determine whether they followed a normal distribution. For normally distributed data, ANOVA and paired sample t-tests were conducted to evaluate significant differences

between groups. For non-normally distributed data, non-parametric tests, including the Kruskal-Wallis test, Wilcoxon test, and Mann-Whitney test, were employed. All statistical analyses were performed using SPSS software version 25 (IBM Corp, Armonk, NY, USA), and results were considered statistically significant at $p<0.05$.

Results and Discussion

This study examined the antidiabetic effects using enzymatic methods, including oral glucose tolerance tests and blood glucose level measurements performed with a glucometer operating on an electrochemical principle. The glucometer's operation is based on measuring the potential (electric power) generated by the reaction between glucose and reactive substances on the electrode strip. Blood samples are absorbed by the test strip via capillary action. When blood enters the reaction chamber of the test strip, potassium ferricyanide is broken down, and the glucose in the sample is oxidised by glucose oxidase enzymes, resulting in the reduction of potassium hexacyanoferrate (III) to potassium hexacyanoferrate (II). A constant voltage from the measuring device reconverts potassium hexacyanoferrate (II) back to potassium hexacyanoferrate (III), producing electrons. The number of electrons generated is proportional to the glucose concentration in the sample. After 10 seconds, the glucose concentration is displayed on the monitor screen.[18]

This study observed changes in blood glucose levels after diabetic mice were treated with herbal infusion preparations. Diabetes was induced in the mice using streptozotocin (STZ). STZ is commonly used in experimental studies due to its ability to damage pancreatic *β*-cells, leading to insulin-dependent diabetes mellitus (IDDM), also known as type 1 diabetes mellitus (T1DM). STZ-based protocols are extensively applied in mice and rats to develop models of insulin deficiency and hyperglycemia. These animal models are pivotal for investigating the underlying mechanisms of T1DM, evaluating new therapeutic approaches, and assessing treatment options for the condition.[19]

After hyperglycemia was confirmed three days following STZ induction, the mice began receiving treatments from day 0 to day 21. Blood samples were collected for testing on days 0, 7, 14, and 21 using a glucometer. The glucometer was selected due to its ease of use, practicality, speed, and minimal blood volume requirement (approximately 0.3–1 µL), in contrast to other methods involving instruments like spectrophotometers and multiple chemical reagents for reduction and condensation.

Antidiabetic Testing of Herbal Infusion of Bay Leaves, Sambiloto Herb, and Brotowali Stems

In Table 1, results reveal that all doses-including 1.95 g/20 gBW, 3.9 g/20 gBW, and 7.8 g/20 gBW-as well as the positive control (metformin, 1.3 mg/20 gBW) and the negative control showed a significant increase in blood glucose levels at H0 compared to pre-induction values. The groups receiving herbal infusions at doses of 1.95 g/20 gBW, 3.9 g/20 gBW, and 7.8 g/20 gBW, along with the positive control group, displayed a gradual reduction in blood glucose levels after H0, whereas the negative control group initially showed a slight decrease at H7, followed by a continued increase up to H21 (Table 1). This indicates a significant antidiabetic effect across all tested doses. The reduction in blood glucose levels can be attributed to the therapeutic response of the active compounds in the herbal infusion, which may enhance insulin sensitivity or reduce insulin resistance. *Andrographis paniculata* contains andrographolide, a compound shown to exhibit anti-inflammatory effects and improve enzymatic activity involved in glucose metabolism,[20] *Syzygium polyanthum* leaves are known to contain flavonoids, which assist in controlling blood glucose levels,[21] while *Tinospora crispa* stems contain alkaloids that play a role in enhancing insulin secretion.[22]

The positive control group treated with metformin also demonstrated a gradual reduction in blood glucose levels, consistent with metformin's mechanism of action in reducing hepatic glucose production and improving peripheral insulin sensitivity.[23]

Table 1: Blood Glucose Levels in Male Mice Induced diabetes with STZ, Treated with Herbal Infusion of Bay Leaves, Sambiloto Herb, and Brotowali Stems

Dose	Mean ± Standard Deviation				
	Before Induction	H0	H7	H14	H21
1.95 g/20 gBW	78.00 ± 12.21	414.40 ± 51.19	88.80 ± 12.70	76.00 ± 11.00	64.00 ± 9.30
3.9 g/20 gBW	83.60 ± 14.48	362.40 ± 81.26	123.20 ± 44.18	89.60 ± 14.84	73.60 ± 5.73
7.8 g/20 gBW	72.60 ± 31.85	291.60 ± 65.59	127.80 ± 49.93	90.80 ± 25.61	74.40 ± 10.19
Metformin 1.3 mg/20 gBW (Positive Control)	84.20 ± 11.14	402.60 ± 30.50	239.60 ± 78.64	93.00 ± 23.23	67.40 ± 18.23
Negative Control	57.60 ± 9.13	232.00 ± 59.33	190.20 ± 10.76	191.00 ± 15.38	194.80 ± 16.72

However, the rate of glucose reduction in the positive control group was slower compared to the groups treated with herbal infusions, suggesting that herbal treatments may have a quicker or stronger effect on lowering blood glucose levels. This finding opens the possibility of combining herbal and pharmacological therapies to achieve more rapid glucose control in diabetic patients. In contrast, the negative control group exhibited a steady increase in blood glucose levels by H21, highlighting the progression of diabetes without effective treatment.

Parametric testing using the Shapiro-Wilk normality test indicated that the data were not normally distributed, as the group receiving 7.8 g/20 gBW on day 7 and the positive control group at day 21 had significance values of < 0.05, specifically 0.008 and 0.021, respectively. Homogeneity testing showed that all data had significance values ≥ 0.05, indicating homogeneity. However, due to the lack of normal distribution, non-parametric testing was conducted using the Kruskal-Wallis test, followed by the Wilcoxon and Mann-Whitney tests. The Kruskal-Wallis test results showed that all groups had significance values < 0.05, indicating statistically significant differences among the groups. Further analysis was performed using the Wilcoxon and Mann-Whitney methods.

In Table 2, results of the Wilcoxon test revealed a significant difference ($p < 0.05$) between blood glucose levels before induction and on day 0 across all groups, confirming that STZ induction successfully established diabetic conditions in the mice.[24]

Table 2: Significance Values of Pre- and Post-Test Blood Glucose Levels for the Infusion of Bay Leaves, Sambiloto Herb, and Brotowali Stems

Group	Pre- & Post-Test Comparison			
	H0	H7	H14	H21
1.95 g/20 gBW	0.042*	0.078	0.588	0.144
3.9 g/20 gBW	0.043*	0.138	0.500	0.345
7.8 g/20 gBW	0.043*	0.043*	0.138	0.225
Positive Control	0.043*	0.043*	0.273	0.080
Negative Control	0.043*	0.043*	0.043*	0.043*

*Wilcoxon Test (Significant if p-value < 0.05)

On day 7, a significant reduction in blood glucose levels was observed at the dose of 7.8 g/20 gBW and the positive control group, demonstrating the effectiveness of the herbal infusion and metformin in lowering blood glucose levels. By day 14, the negative control group also exhibited a significant reduction ($p < 0.05$), despite only receiving physiological NaCl, which may have been influenced by the physiological factors of the mice. However, this effect was more limited compared to the groups treated with herbal infusions or metformin. On day 21, while the blood glucose reduction in the negative control group remained significant ($p < 0.05$), it was insufficient to manage long-term diabetic conditions without active therapy. Blood glucose levels in this group tended to rise again, highlighting the importance of active treatment in long-term diabetes management. Subsequently, data analysis proceeded with the Mann-Whitney test.

In Table 3, the Mann-Whitney test results showed a significant difference ($p < 0.05$) in blood glucose levels between the positive control and negative control groups on days 14 and 21. This indicates that metformin effectively reduced blood glucose levels in mice during these days, highlighting its stronger role in glucose regulation compared to physiological NaCl administered to the negative control group.[25] Although there was a reduction in blood glucose in the negative control group, its effect was far more limited.

Table 3: Significance Values for Blood Glucose Levels in Mice Treated with Bay Leaf, Sambiloto Herb, and Brotowali Stem Herbal Infusion

Groups	Significance Values for Blood Glucose Levels in Male Mice				
	Before Induction	H0	H7	H14	H21
A : B	0.402	0.347	0.251	0.209	0.142
A : C	0.075	0.028*	0.047*	0.344	0.209
A : D	0.465	0.0754	0.009*	0.248	0.753
A : E	0.009*	0.009*	0.009*	0.009*	0.009*
B : C	0.047*	0.251	0.917	0.834	0.916
B : D	0.675	0.527	0.028*	0.917	0.116
B : E	0.047*	0.047*	0.047*	0.009*	0.009*
C : D	0.028*	0.036*	0.028*	1.000	0.173
C : E	0.753	0.251	0.116	0.009*	0.009*
D : E	0.009*	0.009*	0.401	0.009*	0.009*

Notes: A: 1.95 g/20 gBW; B: 3.9 g/20 gBW; C: 7.8 g/20 gBW; D: Metformin 1.3 mg/20 gBW (Positive Control); E: (physiological NaCl) (Negative Control) *Significant if p-value < 0.05, determined using Mann-Whitney test

On days 7, 14, and 21, the negative control group receiving only Na-CMC showed significant differences compared to groups treated with herbal infusions at the dose of 1.95 g/20 gBW, 3.9 g/20 gBW, and 7.8 g/20 gBW ($p < 0.05$). The reduction in blood glucose at the dose of 1.95 g/20 gBW and 3.9 g/20 gBW indicates the therapeutic potential of the herbal formulation in improving diabetic conditions. Furthermore, on days 14 and 21, the dose of 7.8 g/20 gBW group demonstrated a more pronounced decrease in blood glucose compared to the negative control group, confirming that higher doses produce stronger effects in reducing blood glucose levels.[26][NO_PRINTED_FORM]

On day 7, significant differences were observed between the positive control group and all dosage groups (1.95 g/20 gBW, 3.9 g/20 gBW, and 7.8 g/20 gBW) ($p < 0.05$). This suggests that the herbal infusion, regardless of dosage, significantly reduced blood glucose after one week of administration. Although metformin provided a faster reduction, the herbal formulation, especially at the dose of 7.8 g/20 gBW, also demonstrated strong potential. On day 7, a significant difference was noted between the groups receiving 1.95 g/20 gBW and 7.8 g/20 gBW ($p < 0.05$), indicating the greater efficacy of higher doses in lowering blood glucose. However, there were no significant differences ($p > 0.05$) between the groups receiving 1.95 g/20 gBW and 3.9 g/20 gBW or between those receiving 3.9 g/20 gBW and 7.8 g/20 gBW, suggesting that the dose of 3.9 g/20 gBW was sufficient to achieve maximum efficacy in lowering blood glucose levels.[27] Increasing the dose beyond this did not significantly enhance the effect.

Antidiabetic Testing of Jamblang Bark Infusion

The average blood glucose levels of mice in each group were measured before induction, and on days 0, 7, 14, and 21. On day 0, which was three days post-STZ injection , all mice developed hyperglycaemia with blood glucose levels >200 mg/dL, confirming the efficacy of STZ in inducing diabetes as per preliminary dose testing. From day 0 to day 7, all dosage groups experienced a reduction in blood glucose levels, indicating antidiabetic activity. In contrast, the negative control group showed neither significant increase nor decrease in blood glucose, as these mice were only induced diabetes with STZ and received no treatment.

Metformin successfully stimulated insulin secretion, leading to a reduction in blood glucose levels from day 0 to day 21. The infusion dose of 2.06 g/20 gBW was the most effective in reducing blood glucose levels in mice by day 21. Data revealed that the dose of 2.06 g/20 gBW infusion could lower blood glucose levels to initial levels or even lower. Meanwhile, the dose of 1.47 g/20 gBW and 1.76 g/20 gBW infusions reduced blood glucose until day 14 but showed a rebound increase by day 21. The average reduction in blood glucose levels suggests that higher doses of the infusion result in more significant glucose reductions, making the 2.06 g/20 gBW dose an optimal choice for lowering blood glucose.

The reduction in glucose levels with the jamblang bark (*Syzygium cumini* L.) infusion is attributed to its flavonoid and tannin content, which act as secondary metabolites with antidiabetic properties. Flavonoids exhibit antioxidant properties due to their phenolic -OH groups, stabilising free radicals by donating hydrogen atoms, thereby reducing oxidative damage to pancreatic β-cells caused by Reactive Oxygen Species (ROS).[28] This supports β-cell recovery and insulin release stimulation.[29] Tannins and flavonoids enhance glucose and lipid metabolism while preventing their accumulation.

Tannins, as astringent agents, shrink the epithelial membrane of the small intestine, reducing nutrient absorption, including sugars, and thus inhibiting blood glucose elevation.[30] Tannins also act as antioxidants, stabilising free radicals by donating electrons from their phenolic -OH groups to oxidative compounds.[31] Therefore, both flavonoids and tannins play a significant role in lowering blood glucose levels, with mechanisms similar to sulfonylurea hypoglycaemic drugs, such as enhancing pancreatic insulin secretion.

In Table 4, which presents the mean and standard deviation of blood glucose levels in mice administered with Jamblang bark infusion across different doses and time points, notable changes in glucose levels were observed over the study period. Based on the results of the parametric test using the Shapiro-Wilk normality test, the data was found not to be normally distributed. The data for the dose of 2.06 g/20 gBW on day 0 and day 14, and the positive control group on day 21 had significance values of <0.05, specifically 0.011, 0.023, and 0.021, respectively. These results indicate that the data does not follow a normal distribution. Consequently, a non-parametric test was conducted, starting with the Kruskal-Wallis test, followed by the Wilcoxon and Mann-Whitney tests. The Kruskal-Wallis test results revealed that all groups had significance values of <0.05, indicating that the data showed significant differences among the groups. Further data analysis was performed using the Wilcoxon and Mann-Whitney methods.

Based on the data analysis presented in Table 5 using the Wilcoxon method, significant differences were observed in several comparisons. A notable difference ($p < 0.05$) was found between blood glucose levels before induction and on day 0 across all groups, indicating the impact of the induction process. Similarly, a significant difference ($p < 0.05$) was observed between blood glucose levels before induction and on day 7 in all groups, reflecting the effectiveness of the treatments administered. Furthermore, a significant difference ($p < 0.05$) was identified between blood glucose levels before induction and on day 14, specifically in the dose of 1.76 g/20 gBW and the negative control

group. Additionally, on day 21, a significant difference ($p < 0.05$) was noted between blood glucose levels before induction and those in the negative control group. These findings highlight the varying effects of the treatments over time. Subsequent data analysis was carried out using the Mann-Whitney method.

Table 4: Blood Glucose Levels in Mice Administered Jamblang Bark Infusion

Dose	Mean ± Standard Deviation				
	Before Induction	H0	H7	H14	H21
1.47 g/20 gBW	74.20 ± 16.38	231.60 ± 148.39	120.00 ± 26.50	93.80± 23.18	72.40 ± 10.21
1.76 g/20 gBW	27.18 ± 3.97	445.60 ± 107.78	167.80 ± 40.23	116.00 ± 28.40	82.40 ± 11.78
2.06 g/20 gBW	27.60 ± 2.47	244.40 ± 138.72	129.20 ± 28.22	88.40 ± 17.64	71.40 ± 13.33
Positive Control	84.20 ± 11.14	402.60 ± 30.50	239.60 ± 78.64	93.00 ± 23.23	67.40 ± 18.23
Negative Control	57.60 ± 9.13	232.00 ± 59.33	190.20 ± 10.76	191.00 ± 15.38	194.80 ± 16.72

Table 5: Significance Values of Pre- and Post-Test Blood Glucose Levels for Jamblang Bark Infusion

Group	Pre- and Post-Test Comparison			
	H0	H7	H14	H21
1.47 g/20 gBW	0.043*	0.043*	0.080	0.498
1.76 g/20 gBW	0.043*	0.043*	0.043*	0.225
2.06 g/20 gBW	0.043*	0.043*	0.893	0.138
Positive control	0.043*	0.043*	0.273	0.080
Negative control	0.043*	0.043*	0.043*	0.043*

*Significance tested using Wilcoxon (Significant if p-value < 0.05).

Based on Table 6, The Mann-Whitney test results revealed significant differences among several groups. On days 0 and 7, the dose of 1.47 g/20 gBW exhibited significant differences compared to the dose of 1.76 g/20 gBW ($p < 0.05$), indicating that higher doses had a stronger glucose-lowering effect. Additionally, on day 7, the dose of 1.47 g/20 gBW also demonstrated significant differences compared to the positive control group (metformin), although the effect was not as pronounced as that of metformin. The negative control group, which did not receive any intervention, experienced a significant increase in blood glucose levels on days 7, 14, and 21 ($p < 0.05$). In contrast, groups treated with herbal infusions at the dose of 1.47 g/20 gBW, 1.76 g/20 gBW, and 2.06 g/20 gBW showed significant reductions in blood glucose levels. No significant differences were observed between the dose of 1.47 g/20 gBW, 1.76 g/20 gBW, and 2.06 g/20 gBW, indicating that the dose of 1.47 g/20 gBW already achieved maximal efficacy. These findings support the potential of herbal infusions as an alternative treatment for diabetes, with the 1.47 g/20 gBW dose emerging as an effective option.[16]

Table 6: Significance Values of Blood Glucose Levels in Mice Administered Jamblang Bark Infusion

Groups	Significance Value of Male Mice Blood Glucose Levels				
	Before Induction	H0	H7	H14	H21
A : B	0.754	0.047*	0.047*	0.207	0.175
A : C	0.295	0.602	0.917	0.916	0.753
A : D	0.209	0.117	0.009*	0.753	0.207
A : E	0.142	0.602	0.009*	0.009*	0.009*
B : C	0.076	0.047*	0.117	0.047*	0.207
B : D	0.142	0465	0.175	0.117	0.116
B : E	0.076	0.009*	0.401	0.009*	0.009*
C : D	1.000	0.117	0.016*	0.917	0.248
C : E	0.021*	0.602	0.016*	0.009*	0.009*
D : E	0.009*	0.009*	0.421	0.009*	0.009*

Notes: A: 1.47 g/20 gBW; B: 1.76 g/20 gBW; C: 2.06 g/20 gBW; D: Metformin 1.3 mg/20 gBW (Positive Control); E: (physiological NaCl) (Negative Control)
*Significant differences were determined using the Mann-Whitney test ($p < 0.05$).

Conclusion

The infusion of herbal remedies (bay leaves (*Syzygium polyanthum*), sambiloto herb (*Andrographis paniculata* Ness), brotowali stems (*Tinospora crispa* L.)), and the infusion of jamblang bark (*Syzygium cumini*) demonstrated effectiveness in lowering blood glucose levels in male mice induced diabetes with streptozotocin, highlighting their potential as antidiabetic agents with statistically significant outcomes. Further clinical investigations are warranted to confirm these findings and to explore the therapeutic dosage, safety profiles, and long-term effects of these herbal preparations in diabetic patients.

Conflict of Interest

The author`s declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

Acknowledgements

The authors express their gratitude to the Research and Community Service Institute (LPPM) of Universitas Singaperbangsa Karawang for their support.

References

1. Sholih MG, Muhtadi A, Saidah S. Cost of Illness Analysis of Insulin Therapy and Insulin–Metformin Combination Therapy in Type 2 Diabetes Mellitus Patients at a Hospital in Bandung. Indones J Clin Pharm. 2018;7(1):10-18. doi:https://doi.org/10.15416/ijcp.2018.7.1.10
2. Arwie D, Sarmila S, Ridwan A, Aryandi R, Islawati I. Identification of *C. albicans* in the Urine of Diabetes Mellitus Patients at Griya Sehat Link Care, Bulukumba Regency. PharmaCine: J Pharm Med Health Sci. 2025;6(1):28-36. doi:https://doi.org/10.35706/pc.v6i1.53
3. International Diabetes Federation. IDF Diabetes Atlas. 10th Ed.; 2021. Accessed June 27, 2025. https://diabetesatlas.org/
4. Wahidin M, Achadi A, Besral B, Kosen S, Nadjib M, Nurwahyuni A, Ronoatmodjo S, Rahajeng E, Pane M, Kusuma D. Projection of diabetes morbidity and mortality till 2045 in Indonesia based on risk factors and NCD prevention and control programs. Sci Rep. 2024;14(1):1-17. doi:https://doi.org/10.1038/s41598-024-54563-2
5. American Diabetes Association. 2. Classification and diagnosis of diabetes: Standards of medical care in diabetes-2021. Diabetes Care. 2021;44(Suppl 1):S15-S33. doi:https://doi.org/10.2337/dc21-s002
6. Pratama R, Nurasih W, Asnawi A, Suhardiman A, Zaelani D, Pahlevi MR. Development and Standardization of an Effervescent Granule Formulation of Pomegranate Peel Extract with Potential Antioxidant Activity. Trop J Nat Prod Res. 2025;9(3):1112-1117. doi:https://doi.org/10.26538/tjnpr/v9i3.28
7. Dewi I, Chodidjah C, Hussaana A. Evaluation of Clitoria ternatea L. Flower Extract in Preventing Complications of Diabetes Mellitus. Trop J Nat Prod Res. 2023;7(10):4908-4911. doi:http://www.doi.org/10.26538/tjnpr/v7i10.28
8. Kurniawan N, Rozikin, Saputra IPBA, Sabariah, Kresnapati INBA. Effectiveness of Bay Leaf Decoction (*Syzygium polyanthum*) on Reducing Blood Glucose Levels in Paok Motong, Masbagik, East Lombok. Curr Biochem. 2023;10(2):52-61. doi:https://doi.org/10.29244/cb.10.2.2
9. Rahim NSM, Ahmad IF, Tan TYC. Potential of *syzygium polyanthum* (Bay leaf) in lowering blood glucose level: A review. Pertanika J Sci Technol. 2021;29(4):2261-2277. doi:https://doi.org/10.47836/pjst.29.4.02
10. Akhtar MT, Sarib MSBM, Ismail IS, Abas F, Ismail A, Lajis NH, Shaari K. Anti-Diabetic Activity and Metabolic Changes Induced by *Andrographis paniculata* Plant Extract in Obese Diabetic Rats. Molecules. 2016;21(8):1026. doi:https://doi.org/10.3390/molecules21081026
11. Koay YC, Amir F. A review of the secondary metabolites and biological activities of *Tinospora crispa* (*Menispermaceae*). Trop J Pharm Res. 2013;12(4):641-649. doi:http://dx.doi.org/10.4314/tjpr.v12i4.30
12. Yusof N, Goh MPY, Ahmad N. Evaluation of the Antidiabetic, Islet Protective and Beta-Cell Regenerative Effects of *Tinospora crispa* (L.). Nat Prod Sci. 2022;28(3):105-114. doi:https://doi.org/10.20307/nps.2022.28.3.105
13. National Agency of Drug and Food Control of the Republic of Indonesia. Formulary of Indonesian Traditional Ethnomedicine Recipes, Volume 3.; 2013.
14. Hidayah H, Ikhtianingsih W, Amal S. The Potential of Jamblang Bark Plants (*Syzygium cumini* (L) Skeels) as Anticancer: A Literature Review. Eureka Herba Indones. 2023;4(4):343-348. doi:https://doi.org/10.37275/ehi.v4i4.95
15. Nguyen LKH, Tran C V., Pham ND, Tran T V. Phytochemical Screening, Antioxidant and Xanthine Oxidase Inhibitory Activities of *Vitis heyneana* Schult. Stem Extracts From Vietnam. Trop J Nat Prod Res. 2023;7(9):3981-3987. doi:http://www.doi.org/10.26538/tjnpr/v7i9.20
16. Tripathi AK, Kohli S. Pharmacognostical standardization and antidiabetic activity of *Syzygium cumini* (Linn.) barks (*Myrtaceae*) on streptozotocin-induced diabetic rats. J Complement Integr Med. 2014;11(2):71-81. doi:https://doi.org/10.1515/JCIM-2014-0011
17. Ajiningrum PS, Amilah S, Kurela WA. Effectiveness Test of Juwet Leaf Extract and Juwet Cortex Against Desreasing Blood Glucose Levels of Hiperglemic Mice. J Pharm Sci. 2021;6(2):115-118.
18. Zhang L, Gu C, Ma H, Zhu L, Wen J, Xu H, Liu H, Li L. Portable glucose meter: trends in techniques and its potential application in analysis. Anal Bioanal Chem. 2019;411(1):21-36. doi:http://dx.doi.org/10.1007/s00216-018-1361-7
19. Wu KK, Huan Y. Streptozotocin-Induced Diabetic Models in Mice and Rats. Curr Protoc Pharmacol. 2008;40(1):5.47.1-5.47.14. doi:https://doi.org/10.1002/0471141755.ph0547s40
20. Nugroho AE, Andrie M, Warditiani NK, Siswanto E, Pramono S, Lukitaningsih E. Antidiabetic and antihiperlipidemic effect of *Andrographis paniculata* (Burm. f.) Nees and andrographolide in high-fructose-fat-fed rats. Indian J Pharmacol. 2012;44(3):377-381. doi:https://doi.org/10.4103/0253-7613.96343
21. Widyawati T, Yusoff NA, Asmawi MZ, Ahmad M. Antihyperglycemic Effect of Methanol Extract of *Syzygium polyanthum* (Wight.) Leaf in Streptozotocin-Induced Diabetic Rats. Nutrients. 2015;7(9):7764-7780. doi:https://doi.org/10.3390/nu7095365
22. Zuhri UM, Purwaningsih EH, Fadilah F, Yuliana ND. Network pharmacology integrated molecular dynamics reveals the bioactive compounds and potential targets of *Tinospora crispa* Linn. as insulin sensitizer. PLoS One. 2022;17(6):e0251837. doi:https://doi.org/10.1371/journal.pone.0251837
23. Tamura Y, Watada H, Sato F, Kumashiro N, Sakurai Y, Hirose T, Tanaka Y, Kawamori R. Effects of metformin on peripheral insulin sensitivity and intracellular lipid contents in muscle and liver of overweight Japanese subjects. Diabetes Obes Metab. 2008;10(9):733-738. doi:https://doi.org/10.1111/j.1463-1326.2007.00801.x
24. Furman BL. Streptozotocin-Induced Diabetic Models in Mice and Rats. Curr Protoc Pharmacol. 2015;70:5.47.1-5.47.20. doi:https://doi.org/10.1002/0471141755.ph0547s70
25. Horakova O, Kroupova P, Bardova K, Buresova J, Janovska P, Kopecky J, Rossmeisl M. Metformin acutely lowers blood glucose levels by inhibition of intestinal glucose transport. Sci Rep. 2019;9:6156. doi:https://doi.org/10.1038/s41598-019-42531-0
26. Isioye IO, Akindele AJ, Aigbe FR, Olatoye FJ, Olaleye O, Sofidiya MO, Sowemimo A, Akande IS. Effects of Hydroethanolic Rhizome Extract of *Anchomanes difformis* (Blume) in Type 2 (Streptozocin-Nicotinamide-Induced) Diabetic Rats. Trop J Nat Prod Res. 2024;8(1):6016-6026. doi:http://www.doi.org/10.26538/tjnpr/v8i1.44
27. Wang HJ, Chiang BH. Anti-diabetic effect of a traditional Chinese medicine formula. Food Funct. 2012;3(11):1161-1169. doi:https://doi.org/10.1039/C2FO30139C
28. Baldissera G, Sperotto NDM, Rosa HT, Henn JG, Peres VF, Moura DJ, Roehrs R, Denardin ELG, Dal Lago P, Nunes RB,

Saffi J. Effects of crude hydroalcoholic extract of *Syzygium cumini* (L.) Skeels leaves and continuous aerobic training in rats with diabetes induced by a high-fat diet and low doses of streptozotocin. J Ethnopharmacol. 2016;194:1012-1021. doi:https://doi.org/10.1016/j.jep.2016.10.056

29. Sanches JR, França LM, Chagas VT, Gaspar RS, dos Santos KA, Gonçalves LM, Sloboda DM, Holloway AC, Dutra RP, Carneiro EM, Cappelli APG, Paes AM de A. Polyphenol-Rich Extract of *Syzygium cumini* Leaf Dually Improves Peripheral Insulin Sensitivity and Pancreatic Islet Function in Monosodium L-Glutamate-Induced Obese Rats. Front Pharmacol. 2016;7:48. doi:https://doi.org/10.3389/fphar.2016.00048
30. Pujiastuti E, Nugroho AE, Nisa K, Hertiani T. Revealing the Contribution of Phytochemicals in *Syzygium cumini* as Diabetics: A Systematic Review. Indones J Pharm. 2023;34(4):519-540. doi:https://doi.org/10.22146/ijp.6812
31. Martia E, Mulki MA, Nurfadhila L. Antioxidant Activity Test of Balakacida Leaves (*Chromolaena Odorata* L.) with DPPH (2,2-Difenil-1-Pikrilhidrazil) Method. Analit: Anal Environ Chem. 2024;9(1):36-44.