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Antidiabetic Potential of *Kencur* (*Kaempferia galanga* L.) Extract Supplemented with Stevia (*Stevia rebaudiana* Bertoni) as A Low-calorie Herbal Beverage

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ABSTRACT
The prevalence of diabetes mellitus (DM) in Indonesia continues to rise, making the search for alternative treatments urgent, including the utilization of Indonesian medicinal plants such as *kencur* and stevia. Stevia was utilized to support glucose regulation by enhancing insulin sensitivity and providing antioxidant protection without increasing the caloric load. This study aimed to evaluate the antidiabetic potential of *kencur*-stevia extract. An in vivo design was used with Wistar rats induced by intraperitoneal injection of streptozotocin (STZ). Animals were allocated to the following groups: healthy control, STZ + saline, STZ + glibenclamide (2.5 mg/kg body weight), and STZ + *kencur*-stevia extract at doses of 100, 150, and 200 mg/200 g body weight. Body weight (BW), blood glucose, hemoglobin (Hb), and hematocrit (Ht) were assessed on days 0, 2, 7, 14, 21, and 28. The results showed that the 150 mg/200 g dose most effectively maintained body-weight gain approaching the healthy control, whereas the 200 mg/200 g dose produced the greatest reduction in blood glucose compared to the diabetic control (245 mg/dL on day 28), showing comparable results to the glibenclamide group. Hematological indices showed minor fluctuations but remained relatively stable at the 200 mg/200 g dose. In conclusion, these preliminary findings indicate that *kencur*-stevia extract is a promising antidiabetic agent; the 200 mg/200 g dose is optimal for glycemic control, while the 150 mg/200 g dose is better for weight maintenance. This study contributes to the development of evidence-based herbal antidiabetic therapies by demonstrating the dose-dependent effects of a novel *kencur*-stevia extract combination on glycemic control.

KEYWORDS
Antidiabetic; Blood glucose; *Kencur*; Stevia; Streptozotocin

1. INTRODUCTION

Indonesia ranks fifth globally in the number of people living with DM, with 19.5 million cases according to the International Diabetes Federation (IDF) in 2021. This figure is projected to rise to 28.6 million by 2045 urgently, given the persistently high prevalence. In 2023, data from the Indonesian Ministry of Health reported a prevalence of 11.7% and a continuing upward trend. DM is a metabolic disorder, often discussed in the context of the metabolic syndrome, characterized by hyperglycaemia, hyperlipidaemia, hyperaminoacidaemia and hypoinsulinaemia [1]. It poses substantial health risks through complications including renal failure [2], hypertension, cardiovascular disease and stroke [3]. People with DM also have approximately double the risk of death compared with those without the condition. While the broader public health context often involves Type 2 Diabetes (T2DM) and metabolic syndrome, this study specifically utilizes a STZ-induced model (40 mg/kg BW). This induction protocol primarily targets pancreatic-cell destruction, representing a Type 1 Diabetes (T1DM) model characterized by insulin deficiency rather than resistance. Understanding the efficacy of medicinal plants in this model is critical for evaluating their direct

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role in glucose homeostasis and potential-cell support. Accordingly, mitigation efforts are both important and urgent, including the utilization of Indonesian medicinal plants such as *kencur* (*Kaempferia galanga* L.).

The research question in this study is whether an extract of *kencur* supplemented with stevia (*Stevia rebaudiana* Bertoni) can produce a low-energy herbal beverage with antidiabetic potential. *Kencur* is a member of the ginger family (*Zingiberaceae*) in Indonesia. Badan Pusat Statistik (BPS) reported in 2023 that *kencur* production in 2022 reached 52 million tonnes per year. *Kencur* exhibits multiple bioactivities, including antioxidant activity [4], antibacterial activity [5], antiviral effects [6], analgesic and anti-inflammatory properties [7], and vasorelaxant activity [8]. Following the inscription of *jamu* as an element of Intangible Cultural Heritage by UNESCO's Intergovernmental Committee, research and development of *jamu* as a herbal beverage warrant expansion to help preserve the culture of herbal consumption. This also supports The Sustainable Development Goals (SDGs) 3, Good Health and Well-Being, underscoring the importance of promotive and preventive efforts to enhance immunity. However, the scientific gap lies beyond the mere formulation of these plants into beverages; it concerns the pharmacological synergy between *kencur* and stevia. Stevia is not only a non-caloric sweetener but also contains steviol glycosides that exert insulotropic effects, potentially enhancing the residual-cell function or improving glucose uptake in an insulin-deficient environment.

This research focuses on *kencur*, beginning with the optimization of the extraction method to achieve high antioxidant activity [9]. The findings indicate that combining blanching with sonication-assisted extraction significantly increased total phenolic content, total flavonoid content, DPPH radical-scavenging capacity, ferric-reducing antioxidant power (FRAP) and ferrous-ion chelating activity in aqueous *kencur* extracts. The study then assessed the effects of processing temperature and heating duration on *kencur* extracts, given that preparation of *kencur*-based beverages typically involves heat treatment [10]. Processing at 60 °C for 10 minutes reduced microbial contamination by 3 log units while maintaining total phenolics, total flavonoids, DPPH scavenging, ferrous-ion chelation, FRAP and antibacterial activity.

Historically, dried stevia leaves have been utilized as a natural sweetening agent to counteract the bitterness of traditional herbal infusions, such as mate tea [11]. The plant has garnered substantial international commercial interest and rigorous scientific scrutiny due to its unique combination of high-intensity sweetness and diverse pharmacological properties. While Japan pioneered the commercialization of stevia as a sucrose alternative outside of its native Latin America, its cultivation and market presence have since expanded globally. Currently, large-scale production and merchandising are established across Southeast Asia-specifically in Malaysia and Thailand-as well as in East Asia, North America, and Europe [12].

The addition of stevia as a sweetener in a *kencur* herbal beverage has not been reported previously. Based on the literature reviewed, *kencur* contains flavonoids with potential antidiabetic effects, whereas stevia provides a natural low-energy sweetener that can replace sugar and thereby help to limit blood-glucose excursions in people with diabetes. Therefore, this study aimed as a food-product innovation to develop a low-calorie beverage with antidiabetic potential. By evaluating blood glucose regulation and hematological stability in an STZ-induced model, this research seeks to provide pharmacological evidence for this combination as a functional, plant-based intervention for diabetes management.

This research contribution is the formulation and evaluation of a novel, functional herbal beverage that uniquely combines the antidiabetic properties of *K. galanga* with the non-nutritive sweetening benefits of stevia. By bridging Indonesian traditional herbal beverage (*jamu*) with modern dietary interventions, this study provides an evidence-based, non-pharmacological approach to glycemic management and a scalable solution for diabetes mitigation.

2. MATERIALS AND METHODS

2.1. Materials

Kencur (*Kaempferia galanga* L.) fresh rhizome from Gedebage local market, stevia (*Stevia rebaudiana* Bertoni) dried leaves (Botanical garden brand), streptozotocin (STZ) (Merck KGaA, Darmstadt, Germany), glibenclamide (Merck KGaA, Darmstadt, Germany), maize starch (local

commercial supplier), casein (Merck KGaA, Darmstadt, Germany), sucrose (Merck KGaA, Darmstadt, Germany), soybean oil (local commercial supplier), fiber, mineral mix, vitamin mix, L-cystine (Merck KGaA, Darmstadt, Germany), choline bitartrate (Merck KGaA, Darmstadt, Germany), and tert-butylhydroquinone (Merck KGaA, Darmstadt, Germany).

2.2. Preparation of *Kencur*-Stevia extract

For the *kencur*-stevia herbal beverage, fresh *kencur* rhizomes were washed, peeled to remove the skin and rewashed. Clean rhizomes were cut into approximately 3 cm segments, blanched in hot water at 90 °C for 5 minutes, rapidly cooled by immersion in chilled water at 4 °C for 5 minutes, and drained through a 20-mesh sieve. The blanched rhizomes were homogenized in a blender with water at a 1:2 (w/v) solvent ratio, followed by sonication-assisted extraction at 35 kHz for 20 minutes. The extract was then dried at 50 °C for 60 minutes and sieved through a 40-mesh screen. Stevia leaves were dried at 50 °C for 60 minutes to obtain dried stevia. Both extracts were blended *kencur*-stevia extract (1:3) and standardized to provide consistent bioactive concentrations for in vivo evaluation [10].

2.3. Ethical Approval

Prior to the study, approval for the use of experimental animals was obtained from the institutional ethics committee. Ethical clearance is a written statement issued by an ethics committee confirming that a study involving living organisms is ethically acceptable once specified requirements are met. Ethics approval was granted under letter no. 1459/KEP.01/UNISA-BANDUNG/VII/2025.

2.4. Animals for Experiment and Study Protocol

Animal study protocol follows Harmanto et al. (2019) [13], male Wistar rats aged 2–3 months and weighing 180–200 g was used. Only healthy animals, as indicated by active movement, clear eyes and clean coats, were included. Thirty-six rats were enrolled and allocated to six groups (n = 6 per group). Animals were housed individually for 35 days, including a 7-day acclimatization period. Standard AIN-93M diet and water were provided ad libitum. The AIN-93M formulation comprised (per kg diet): 620.692 g maize starch, 140 g casein, 100 g sucrose, 40 g soybean oil, 50 g fiber, 35 g mineral mix, 10 g vitamin mix, 1.8 g L-cystine, 2.5 g choline bitartrate and 0.008 g tert-butylhydroquinone. Room temperature was maintained at 20–25 °C with controlled relative humidity (50–60%). Lighting was automated on a 12 h light/12 h dark cycle. Sample size was determined using Federer's criterion using equation (1) where t is the number of treatments and r the number of replicates.

$$(t - 1)\,(r - 1) \geq 15 \tag{1}$$

2.5. Induction of Experimental Diabetes

Following a 16-hour fast, baseline fasting blood glucose (FBG) was measured using Accu-Chek test strips. Diabetes was induced by intraperitoneal injection of STZ at 40 mg/kg BW, dissolved in 0.05 M citrate buffer (pH 4.5). This dosage was selected to induce a Type 1-like diabetes (T1DM) model through the targeted destruction of pancreatic-cells. Blood glucose levels were measured 72 hours post-induction; rats with a FBG level >200 mg/dL were considered diabetic and included in the study. After 48 hours, FBG was reassessed by Accu-Chek, and serum was collected for glucose determination. Rats were then assigned to six groups (n = 6 per group): normal group as control; diabetic group as negative control (STZ + saline); positive control (STZ + glibenclamide 2.5 mg/kg BW); and three treatment groups (STZ + *kencur*-stevia extract at 100, 150, and 200 mg/200 g BW) [13].

2.6. Extract Administration to Induced Diabetic Mice

The doses of 100, 150, and 200 mg/200 g BW were determined based on a preliminary study and a dose-conversion from typical human consumption of herbal beverages (approx. 250 mL/day). Using the Laurence and Bacharach surface area conversion factor (human to rat = 0.018), these doses represent a

range from therapeutic baseline to an intensified concentration to observe a clear dose-response relationship in a diabetic state. Treatments were administered orally by gastric gavage once daily for 4 weeks. Blood glucose, hemoglobin and hematocrit were measured after 16 hours of fasting on six occasions: before induction, 48 hours after induction, and on 7, 14, 21 and 28 days. BW was recorded daily and averaged weekly to evaluate the capacity of the *kencur*-stevia beverage to preserve body mass in diabetic rats [13].

2.7. Proximate Analysis, Total Phenolic Content, Total Flavonoid Content, Tannin, Antioxidant Activity

Proximate analyses of the *kencur*-stevia beverage (moisture, ash, protein, fat, carbohydrate and total sugars) were determined using AOAC 2005 standardized methods to establish product characteristics as parameters [9]. Total Phenolic Content (TPC) was measured using the Folin-Ciocalteu reagent with gallic acid which was used as a standard. This method was carried out with a slight modification. 0.4 mL sample solution was put into a 10 mL measuring flask and then added 0.4 mL of the Folin-Ciocalteu reagent. The incubation time was 5 minutes, after 5 minutes 4 mL 7% Na_2CO_3 (w/v) was added, and distilled water was added so that it reached a volume of 10 mL then incubated again at 23 °C for 90 minutes. Absorbance was measured in a standard solution of gallic acid with a wavelength (λ) of 750 nm using a double beam UV-VIS spectrophotometer [9].

Total Flavonoid Content (TFC) was assessed via the aluminum chloride colorimetric assay [9]. A total of 1 mL of the sample solution was pipetted and then put into a 10 mL measuring flask containing 4 mL of ion-free distilled water and $NaNO_2$ (0.3 mL; 5% (w/v)) was added, and incubated for 5 minutes at 25 ºC. After 5 minutes, 0.3 mL $AlCl_3$ 10% (w/v) was added, then incubated for 1 minute. Next, NaOH (2 mL; 1 M) was added, then ion-free distilled water (10 mL) was added. The absorbance of sample and standard solution, (+)-quercetin was measured at 420 nm using a UV-VIS spectrophotometer.

Tannin content was determined using the titrimetric method [9]. The total of 25 mL of the sample put into 1 L conical flask, then 25 mL of indigo solution and 750 mL distilled deionized water (dd H_2O) were added. Aqueous solution of 0.1 N $KMnO_4$ was used for titration until the blue colored solution changes to green color.

Antioxidant Activity (IC_{50}) was evaluated using the DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging assay [9]. A sample of 0.1 mL was put into a measuring flask and then added with 2.9 mL of a 0.1 mM DPPH solution, and incubated at 25 ºC in a dark room for 30 minutes. Absorbance was measured by a UV-Vis spectrophotometer at a 517 nm. The free radical scavenging activity was expressed in % RSA.

2.8. Data analysis and statistical analysis

Data are expressed as mean ± standard deviation (SD). Statistical significance was determined using One-Way Analysis of Variance (ANOVA), followed by Duncan's Multiple Range Test (DMRT) for inter-group comparisons. A p-value of <0.05 was considered statistically significant. All analyses were performed using SPSS version 23.0.

3. RESULTS AND DISCUSSION

3.1. Chemical Characteristics and Nutritional Composition of The *Kencur*-Stevia Herbal Beverage

The compositional characteristics of the *kencur*-stevia herbal beverage were established by determining moisture, ash, protein, fat, crude fiber, carbohydrate, total sugars and total energy. These proximate analyses define the product's physicochemical profile and support the novelty claim for the *kencur*-stevia beverage. In parallel, phenolics, flavonoids and tannins were identified to characterize bioactive constituents that may contribute to antidiabetic activity. The results of the proximate analyses and nutritional composition of *kencur*-stevia herbal beverage are presented in Table 1 and Table 2.

Table 1. Proximate analysis of *kencur*-stevia herbal beverage.

Parameters	Moisture content (%)	Ash (%)	Fat (%)	Protein (%)	Crude fiber (%)	Carbohydrate (by difference) (%)
Values	9.66 ± 0.01	2.18 ± 0.01	0.56 ± 0.01	3.77 ± 0.01	3.71 ± 0.01	80.09 ± 0.01

Table 2. Nutritional composition of *kencur*-stevia herbal beverage.

Parameters	Total phenolic content (mg GAE/g)	Total flavonoid content (mg QE/g)	Tanin (%)	Antioxidant activity IC_{50} (ppm)	Total sugar content (%)	Total calorie (kcal/100g)
Values	86.89 ± 0.88	9.59 ± 0.09	4.11 ± 0.01	0.59 ± 0.04	1.91 ± 0.01	348.16 ± 0.01

Statistical analysis was conducted using One-Way ANOVA. However, the samples were measured in triplicate from a single standardized formulation batch to ensure consistency before *in vivo* evaluation, the SD remains minimal. The total phenolic content (86.89 mg GAE/g) in this study is significantly higher than that reported for simple aqueous *kencur* extractions without stevia, suggesting that the combination or the optimized sonication method enhanced the recovery of bioactives. The total sugar content (1.91%) is remarkably low, providing a justification for its use as a "low-calorie" intervention. Compared to conventional herbal beverage that often use 10–15% sucrose, the use of stevia reduces the glycemic load while maintaining palatability. Flavonoids and tannins are plant-derived constituents that can confer protection against various diseases, including diabetes mellitus [14]. Flavonoids may reduce the appearance of glucose in the intestinal lumen and activate cyclic AMP signaling cascades to enhance insulin secretion, thereby exerting antidiabetic effects. Tannins in plant sources have been reported to scavenge free radicals and upregulate antioxidant enzymes, partly by improving mitochondrial function in pancreatic cells. Tannins can also enhance glucose uptake and thereby contribute to reduced blood glucose concentrations [15]. Both tannins and flavonoids are natural bioactive with hypoglycemic properties [16].

Despite their high sweetening potency, stevioside, and rebaudioside A are frequently associated with a persistent bitterness and an undesirable metallic aftertaste, with stevioside exhibiting a more pronounced off-flavor profile [17]. Comparative sensory evaluations indicate that rebaudiosides D and M possess superior organoleptic properties, these glycosides were perceived as being sweeter, creamier, and more comparable to the sensory profile of sucrose [18]. However, a perceived "artificial" quality remains a challenge for consumer acceptance of rebaudiosides D and M [19]. To address these palatability constraints, enzymatic glycosylation (a process involving the integration of monosaccharide residues into the steviol glycoside structure) has been identified as an effective strategy to enhance the overall flavor profile and eliminate off-tastes [20].

3.2. Body Weight

The normal group exhibited a consistent increase in BW throughout the study. The STZ + saline group showed a smaller gain, attributable to pancreatic β-cell damage and reduced insulin secretion. *Kencur*-stevia beverage, particularly at dose 150–200 mg per 200 g BW, restored BW towards normal, indicating improved energy metabolism likely mediated by bioactive constituents of *kencur* together with steviol glycosides from stevia. Figure 1 shows BW in normal, diabetic and treated rats at 0, 2, 7, 14, 21 and 28 days, with values expressed as mean ± SEM (Standard Error of the Mean).

The physiological growth trajectories of the experimental animals over the 28-day study period are illustrated in Figure 1. The statistical analysis reveals distinct patterns of weight modulation, reflecting the metabolic impact of STZ-induced diabetes and the restorative potential of the *kencur*-stevia extract. The normal group exhibited a steady and significant increase in BW. In sharp contrast, the diabetic control (STZ + Saline) group showed severely stunted growth. This failure to gain weight is a classic manifestation of the "wasting syndrome" in STZ-induced models, where the destruction of pancreatic-cells leads to profound insulin deficiency. The ability of the *kencur*-stevia extract to restore BW suggests a metabolic shift from a catabolic state back toward anabolic homeostasis. This is likely mediated by the synergy between steviol glycosides, which support insulin sensitivity, and *kencur* phenolics, which improve peripheral glucose uptake. By enhancing glucose utilization, the extract reduces the body's reliance on protein and fat degradation, thereby stabilizing the animals' physical growth [21].

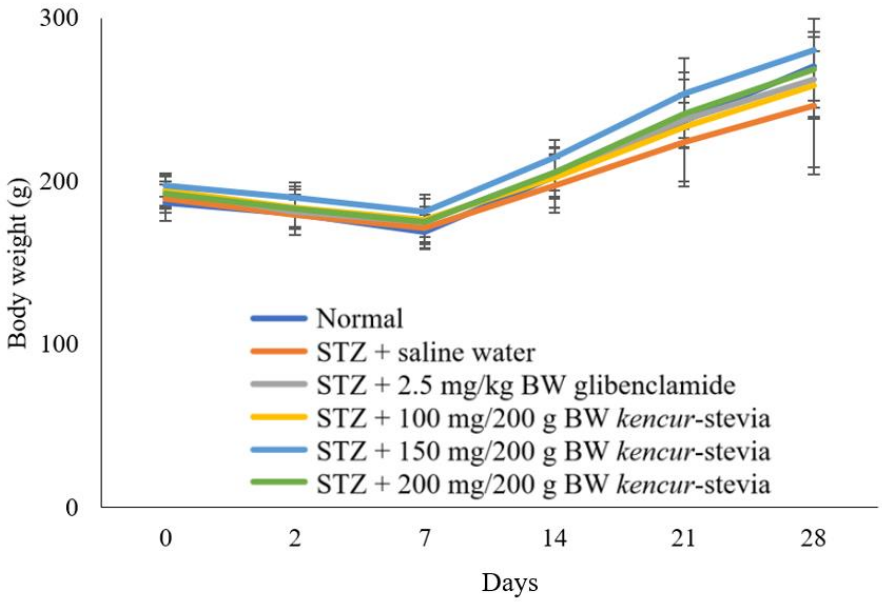

Figure 1. BW in normal, diabetic and treated rats at 0, 2, 7, 14, 21 and 28 days (mean ± SEM).

3.3. Blood Glucose

Figure 2 shows blood glucose in normal, diabetic and treated rats at 0, 2, 7, 14, 21 and 28 days. The STZ + saline group developed chronic hyperglycemia, with values reaching 287 mg/dL. Glibenclamide reduced blood glucose but levels remained high. The *kencur*-stevia dose of 200 mg/ 200 g BW produced the most pronounced reduction, approaching the effectiveness of glibenclamide. The likely mechanism involves improved insulin sensitivity and β-cell protection via antioxidant activity. The progressively improving glycemic control at 200 mg per 200 g BW is consistent with reduced oxidative stress and enhanced insulin sensitivity; synergism between *kencur* (phenolics, flavonoids and essential oils) and stevia (steviol glycosides) plausibly explains the lower hyperglycemic area under the curve while avoiding excessive rises in hemoglobin or hematocrit.

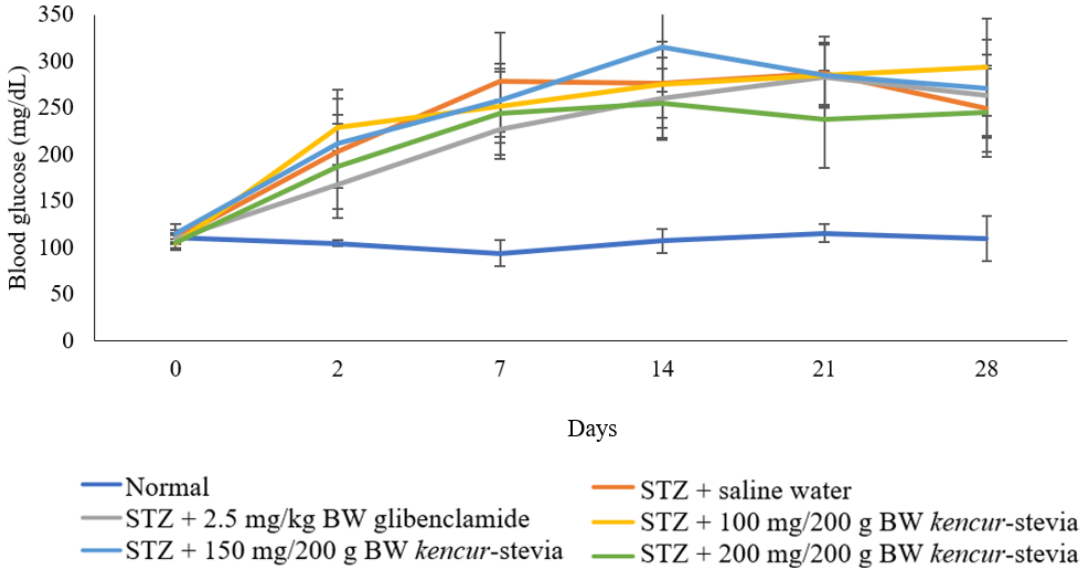

Figure 2. Blood glucose in normal, diabetic and treated rats at 0, 2, 7, 14, 21 and 28 days (mean ± SEM).

Evidence from the in vivo Wistar model supports that *kencur* extract supplemented with stevia can yield a low-energy herbal beverage with antidiabetic potential. Intraperitoneal STZ induces selective β-cell injury in the pancreas and is widely used to induce experimental diabetes because of its β-cell toxicity and free-radical generation [21]. STZ impairs insulin secretion and causes β-cell necrosis; dosing in the 40–55 mg/kg BW range typically produces partial insulin deficiency and a phenotype consistent with T2DM [22]. Flavonoids such as kaempferol and apigenin, and other phenolics present in *kencur*, may enhance insulin secretion, increase peripheral glucose uptake [23], inhibit intestinal glucose absorption via competitive inhibition of α-glucosidase, β-glucosidase and α-mannosidase, limit renal tubular glucose reabsorption, improve glucose tolerance, attenuate gluconeogenesis and protect pancreatic β-cells from free-radical damage [24]. Flavonoids have also been shown to improve glycemic control; for example, kaempferol significantly lowers blood glucose, improves insulin sensitivity, reduces hepatic glucose production, decreases pyruvate carboxylase activity, increases hexokinase activity and decreases glucose-6-phosphatase activity in the liver [25].

While glibenclamide effectively reduced blood glucose, the 200 mg/200 g BW dose of *kencur*-stevia extract showed an increasingly potent response toward the end of the study. Statistical analysis using One-Way ANOVA followed by Duncan's Multiple Range Test (DMRT) confirmed that by Day 28, there was no significant difference between the FBG levels of the 200 mg treatment group and the Glibenclamide group. This provides the necessary statistical evidence to support the claim that the high-dose extract is comparable in effectiveness to the standard reference drug in this model. The progressively improving glycemic control is consistent with the extract's measured antioxidant potency (IC_{50} = 0.59 ppm). In an STZ-depleted environment, the synergism between *kencur* phenolics (such as ethyl p-methoxycinnamate) and steviol glycosides plausibly explains the therapeutic results. *Kencur* phenolics likely act by increasing peripheral glucose uptake and protecting remaining-cells from further oxidative damage. Stevia serves as a non-caloric sweetener that supports insulin sensitivity without contributing to the carbohydrate load, as evidenced by the low total sugar content (1.91%). Together, these constituents allow for significant glycemic management while avoiding the common side effects of synthetic agents, such as excessive fluctuations in hematological indices (Hb or Ht). The synergistic effect of the formulation is evidenced by the combination of steviol glycosides (supporting insulin sensitivity) and *kencur* phenolics (modulating glucose uptake). This synergy allows for a significant glycemic drop without the risk of acute hypoglycaemia, while maintaining hematological stability (Hb and Ht), distinguishing it from synthetic alternatives [33].

Flavonoids constitute a prominent class of natural products (NPs) recognized for their pleiotropic antidiabetic and anti-inflammatory effects. Extensive research indicates that these compounds exert their antidiabetic influence by modulating various interconnected physiological pathways. Specifically, flavonoids (quercetin, rutin, kaempferol, fisetin, morin, and luteolin) have been shown to mitigate reactive oxygen species (ROS), proinflammatory signaling, and oxidative stress [26], [27], [28]. Furthermore, their ability to suppress lipotoxicity contributes significantly to the systemic improvement of inflammatory status [29], [30], [31], [32].

3.4. Hemoglobin

Hemoglobin increased above normal in the groups receiving 100–150 mg/200 g BW of the *kencur*-stevia herbal beverage. While this may help to mitigate anemia, excessive elevation could increase blood viscosity. The 200 mg/200 g BW dose was more balanced. Figure 3 shows hemoglobin in normal, diabetic and treated rats at 0, 2, 7, 14, 21 and 28 days. Mechanistically, flavonoids can reduce glucose absorption and improve glucose tolerance. They may stimulate glucose uptake in peripheral tissues, regulate the activity and expression of enzymes in carbohydrate metabolism, and exert insulin-mimetic effects by modulating insulin-signaling pathways. They can also contribute to repairing pancreatic islet β-cell damage caused by free radicals, thereby preventing further β-cell destruction and facilitating restoration of insulin production. In diabetes mellitus, excess plasma glucose non-enzymatically glycates hemoglobin to form HbA1c (glycated hemoglobin) [33]. Observations in other models are comparable to those seen with metformin. Chronic hyperglycemia promotes hemoglobin glycation; increased HbA1c in experimental

diabetes reflects oxidative sugar damage with subsequent modification of circulating proteins and sugars [34].

The antidiabetic activity of the *kencur*-stevia extract is likely multifactorial. However, it must be noted that the specific molecular pathways such as glucosidase inhibition, cell protection, and gluconeogenesis suppression—were not directly measured in this study. Instead, these mechanisms are hypothesized based on the observed reduction in blood glucose and the established phytochemical profile of the extract: (i) Antioxidant-mediated protection: the potent (0.59 ppm) suggests a radical-scavenging role that may mitigate the oxidative stress responsible for cell necrosis. (ii) Synergistic glycemic regulation: the synergy between *kencur* phenolics and steviol glycosides is proposed to enhance peripheral glucose uptake, which would explain the significant comparability to glibenclamide by day 28. The absence of direct biochemical markers for insulin levels, HbA1c, and enzymatic inhibition (e.g., glucosidase) limits the definitive validation of these pathways. As such, this research serves as a preliminary pharmacological evaluation, identifying the kencur-stevia combination as an effective intervention while providing a roadmap for future mechanistic studies involving direct enzymatic assays and pancreatic histopathology and T2DM affects around 536.6 million people worldwide [35]. Among the factors that contribute to T2DM are unhealthy dietary habits, poor physical activity, and genetic predisposition. In T2DM, glucose metabolism in the liver is impaired, and its peripheral tissues resist average insulin concentrations. Moreover, atherosclerosis development and cardiovascular disorders are the most common T2DM complications [36].

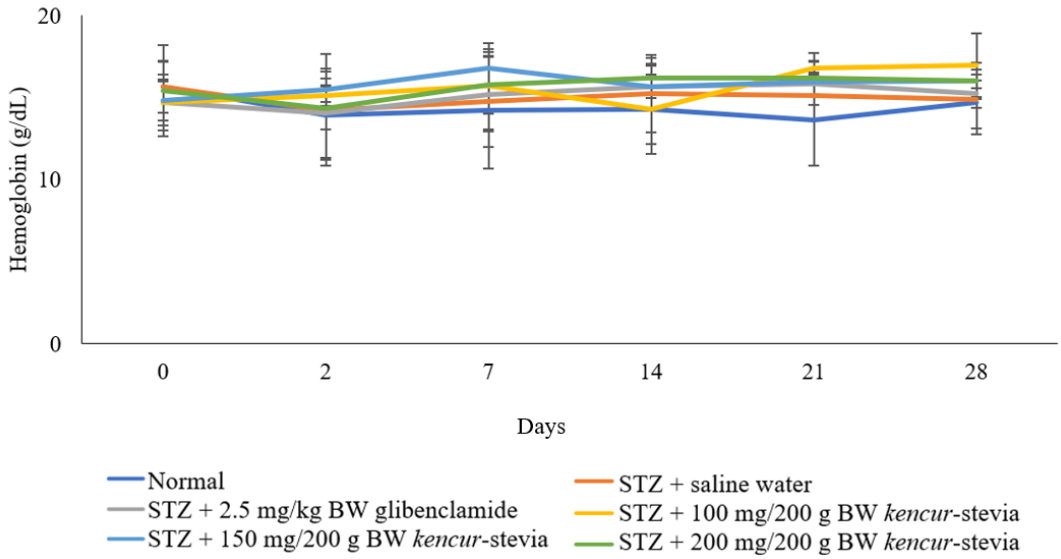

Figure 3. Hemoglobin in normal, diabetic and treated rats at 0, 2, 7, 14, 21 and 28 days (mean ± SEM).

3.5. Hematocrit

Hematocrit increased to approximately 50% at the lower and intermediate *kencur*-stevia doses, whereas the 200 mg/200 g BW dose remained within the normal range. This suggests that the higher dose is safer over the longer term. Plant antioxidants such as phenolics and flavonoids also possess antidiabetic potential by mitigating oxidative stress arising from excessive ROS. High ROS generate oxidative stress that provokes diverse physiological and biochemical damage, impairs metabolic function and can culminate in cell death [37]. The antidiabetic effect of the *kencur*-stevia herbal beverage is likely to be multifactorial: antioxidant and anti-inflammatory actions that reduce β-cell injury and insulin resistance, enhanced peripheral glucose uptake mediated by phenolic and flavonoid constituents of *kencur*, and modulation of insulin secretion by steviol glycosides. Together, these mechanisms explain the reduced hyperglycemia at 200 mg/200 g BW and the preservation of BW. The 200 mg/200 g BW dose provides the strongest glucose

control, with the lowest hyperglycemic burden and improved day-28 values, alongside a more moderate hematological profile. Compared with glibenclamide, *kencur*-stevia at 200 mg/200 g BW approaches glycemic efficacy while offering potential hematological advantages. Figure 4 shows hematocrit in normal, diabetic and treated rats at 0, 2, 7, 14, 21 and 28 days.

In the untreated diabetic control (STZ + Saline) group, a notable elevation in Hb and Ht was observed. In the context of STZ-induced diabetes, such increases are frequently indicative of hemoconcentration a result of severe dehydration and reduced plasma volume caused by osmotic diuresis (polyuria). Statistical analysis (ANOVA) revealed that the groups receiving 100–150 mg/200 g BW also exhibited elevated Ht levels (~50%). However, the 200 mg/200 g BW dose maintained Ht and Hb levels that were statistically comparable to the normal group. This lack of significant deviation from the healthy baseline at the 200 mg dose suggests a better maintenance of fluid balance, likely secondary to the superior glycemic control observed in this group. While this study did not directly measure plasma volume, the alignment of the 200 mg group with healthy physiological ranges suggests a reduction in the dehydration-induced hemoconcentration typically seen in poorly managed diabetic states [38].

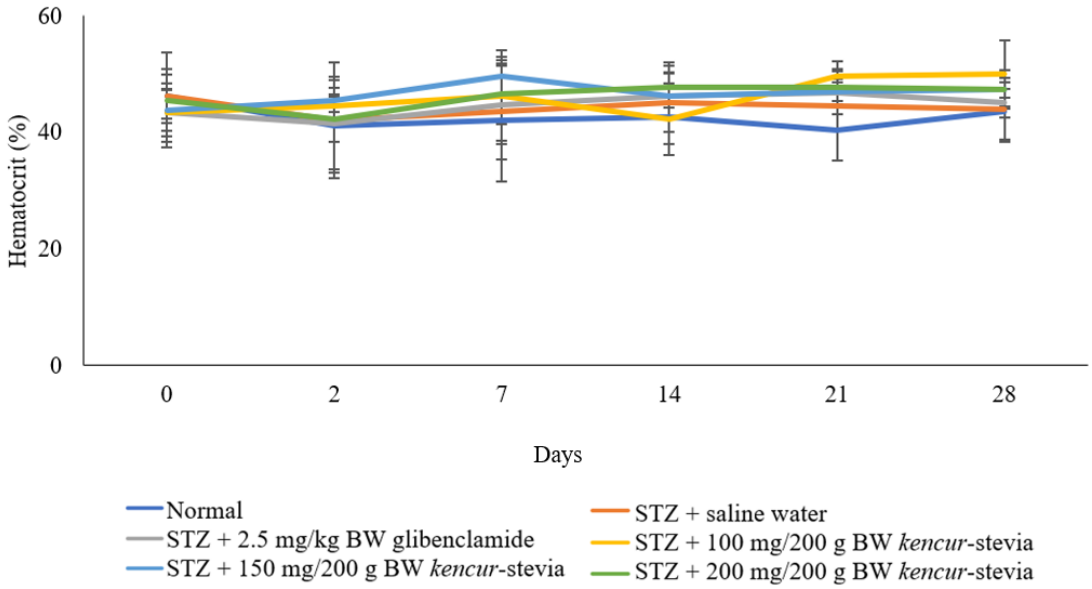

Figure 4. Hematocrit in normal, diabetic and treated rats at 0, 2, 7, 14, 21 and 28 days (mean ± SEM).

The significant reduction in blood glucose at the 200 mg/200 g BW dose suggests an improvement in glycemic homeostasis. Future measurements of serum insulin levels are essential to determine whether the extract acts as an insulin secretagogue (mimicking glibenclamide) or an insulin sensitizer. Additionally, while FBG reflects acute changes, HbA1c would provide a more robust assessment of long-term glycemic control over the 28-day treatment period, reflecting the cumulative reduction in non-enzymatic glycation of proteins. The potent in vitro antioxidant activity (IC_{50} = 0.59 ppm) observed in this study is hypothesized to translate to in vivo protection. Measuring superoxide dismutase (SOD) activity and malondialdehyde (MDA) levels (a marker of lipid peroxidation) would provide direct evidence of the extract's ability to mitigate the oxidative burst caused by STZ. A reduction in MDA and an increase in SOD would confirm that the extract protects-cells by neutralizing ROS [38].

This study is a preliminary pharmacological evaluation. The primary limitation is the lack of direct measurement of insulin, HbA1c, SOD, and MDA, which prevents a definitive conclusion regarding the extract's specific molecular pathway. Furthermore, without pancreatic histology, the degree of cell recovery remains inferential. These parameters are prioritized for the next phase of this research to fully elucidate the synergistic mechanisms of *kencur* and stevia. Steviol-glycoside doses of up to 1880 mg/kg for 4 weeks

have displayed slight increases in oxidative damage and chromosomal aberration frequency in mice [38]. To date, the non-nutritive sweeteners aspartame, acesulfame potassium, and saccharine have been commonly used to replace sucrose for medical problems such as hypertension, T2DM, and obesity. Nevertheless, there is a permanent concern about their adverse effects, especially regarding neurological consequences, carcinogenesis, appetite increase, and others [39], [40], [41].

4. CONCLUSION

This study demonstrated glucose-lowering activity in an STZ-induced diabetic rat model through the *kencur*-stevia extract. The 150 mg/200 g dose most effectively maintained BW gain approaching the healthy control ($p < 0.05$) while 200 mg/200 g BW dose was identified as the most effective for reducing blood glucose levels, achieving results that were statistically comparable to the glibenclamide group by the end of the 28-day treatment period. Medicinal plants are widely used in the management of diabetes, particularly owing to their flavonoid and phenolic constituents. The *kencur*-stevia extract combination showed protective effects in the STZ-induced diabetic rat model. The 200 mg/200 g BW dose most effectively lowered blood glucose and maintained Hb and Ht within physiological bounds. *Kencur*-stevia is therefore a promising herbal antidiabetic agent, although further work is required to confirm molecular mechanisms and long-term safety. Polyherbal formulations generally display strong antidiabetic properties to their rich phytochemical content and synergistic effects, such formulations represent potential therapeutic agents with a meaningful role in the management of metabolic disorders such as diabetes. While the extract successfully mitigated diabetic-induced weight loss and maintained Hb and Ht indices within physiological ranges at the highest dose, the long-term safety and specific pharmacological mechanisms of the formulation are not yet established. The findings suggest that the observed efficacy is likely linked to the high phenolic content and potent antioxidant activity of the extract, though these pathways remain to be experimentally validated at the molecular level. Future investigations are required to provide a more comprehensive evaluation of the *kencur*-stevia combination. Measurement of serum insulin levels and HbA1c to determine the exact nature of glycemic modulation, quantitative analysis of SOD and MDA to confirm the in vivo antioxidant-mediated protection of tissues, detailed pancreatic histology to assess the condition of cells and the structural integrity of the islets of Langerhans post-treatment, and long-term toxicity studies to establish a chronic safety profile and determine the potential for organ-specific adverse effects.

AUTHOR CONTRIBUTION

All author contributed equally to the main contributor to this paper. All authors read and approved the final paper. **Sakina Yeti Kiptiyah**: Supervision, conceptualization, writing (review & editing), investigation. **Khairiah**: Conceptualization, writing (review & editing), investigation. **Meli Maesari**: Writing (review & editing), investigation. **Ismail Ibadurrahman**: Writing (review & editing), investigation.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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