



Effects of Javanese Ginseng (*Talinum paniculatum*) Leaf Decoction on Immunohistochemical Expression and Superoxide Dismutase Levels in Diabetic Rats

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ABSTRACT

Java Ginseng has long been used by Indonesian communities as a medicinal plant and is traditionally consumed as an alternative therapy, even in managing Diabetes Mellitus (DM). The present study aimed to evaluate the effects of the decoction of Javanese ginseng leaf simplicia (DJGLS) on blood glucose levels, serum superoxide dismutase (SOD), the levels and expression intensity of SOD, and pancreatic histopathology in DM rats. Twenty adult male rats were randomly assigned to four groups. The normal control group (GJ-0, n = 5), the DM group (GJ-1, n = 5) received a placebo, and the DM groups (GJ-2, n = 5 and GJ-3, n = 5) were administered a DJGLS (100 g/100 mL, w/v powder simplicia), at volume of 0.5 mL and 1 mL/100 g body weight, respectively for 21 consecutive days. Blood glucose levels were measured using a glucometer. Serum and pancreatic SOD levels were determined using an ELISA kit. Pancreatic histopathology was evaluated using hematoxylin and eosin staining, while pancreatic SOD expression was assessed by immunohistochemical staining. In addition, phytochemical screening was performed on the Javanese ginseng leaf simplicia powder. The present study demonstrated that the phytochemical analysis of Java Ginseng leaf simplicia powder revealed the presence of alkaloids, flavonoids, saponins, tannins, and steroids. DJGLS treatment reduced blood glucose levels and serum SOD levels in diabetic rats, with a significant reduction observed in the GJ-3 group compared with the GJ-1. Administration of DJGLS in the GJ-2 and GJ-3 groups significantly increased pancreatic SOD levels compared with the GJ-1. The DJGLS treatment in the GJ-2 and GJ-3 groups demonstrated restorative effects, as evidenced by the recovery of the Islets of Langerhans area and increased intensity of pancreatic SOD expression compared with the GJ-1. In conclusion, DJGLS treatment was able to reduce blood glucose levels and serum SOD levels, although these values had not fully returned to normal conditions, and it increased pancreatic SOD levels. The DJGLS indicated potential for promoting recovery of the pancreatic Islets of Langerhans area.

Keywords: Decoction, Diabetes, Immunohistochemistry, Javanese ginseng, Superoxide dismutase

INTRODUCTION

A report by the World Health Organization (WHO, 2024) states that in 2022, the prevalence of diabetes among adults aged ≥ 18 years reached approximately 14%, doubling from 7% in 1990. Furthermore, about 59% of individuals aged ≥ 30 years living with diabetes had not received pharmacological therapy, indicating a substantial gap in disease control and management. Diabetes imposes a substantial burden on healthcare systems, with global economic costs estimated to exceed USD 850 billion annually (Parker et al., 2024).

Diabetes mellitus (DM) is a metabolic disorder characterized by hyperglycemia and has become a major global health concern (IDF, 2025). Hyperglycemia triggers oxidative stress due to excessive free radical production through mitochondrial, protein kinase, and hexosamine pathways (Chen et al., 2025). Oxidative stress contributes to the progression of diabetes and organ damage, including the pancreas, by inducing β -cell necrosis, apoptosis, and the release of proinflammatory cytokines (An et al., 2022). The high susceptibility of β -cells to oxidative stress is also associated with reduced activity of antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase (Gerber and Rutter, 2017). Therefore, controlling hyperglycemia by reducing blood glucose levels is crucial to prevent complications.

If hyperglycemia is not adequately controlled, it increases the risk of broader complications, including microvascular disorders such as retinopathy, nephropathy, and neuropathy, as well as macrovascular complications involving atherosclerotic, cardiovascular, cerebrovascular, and peripheral vascular diseases (Tan et al., 2022; IDF, 2025).



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According to Tan et al. (2022), hyperglycemia leads to excessive accumulation of free radicals in cells, resulting in reduced levels of SOD, catalase (CAT), and glutathione peroxidase (GPx).

Traditional medicine has long been utilized and continues to play an important role as an alternative option in healthcare therapy (Yakubu et al., 2020). According to the World Health Organization, approximately 80% of the global population continues to rely on herbal medicine for healthcare needs, particularly in low- and middle-income countries where access to conventional medical services is limited (Badhon, 2023), with the majority of traditional herbal practices originate from well-established medical traditions in China, India, and different regions of Africa (Latif and Nawaz, 2026). The widespread use of traditional medicine is largely attributed to its strong cultural acceptance, its perceived compatibility with the body's physiological conditions, and its relatively lower risk of adverse effects compared with modern pharmaceuticals (Tran et al., 2020).

More than 400 plant species with hypoglycemic activity have been reported (Patel et al., 2012). Nevertheless, the exploration of natural product-based antidiabetic agents remains relevant due to the therapeutic potential of their phytoconstituents in diabetes mellitus management. One such plant is Javanese ginseng (*Talinum paniculatum*), its root infusion has been reported to exhibit hypoglycemic effects in diabetic rats (Jenie and Indraswari, 2021).

Javanese ginseng (*Talinum paniculatum*) has long been empirically utilized by Indonesian communities as a medicinal plant (Susilo et al., 2024). In traditional healing practices, plant parts such as the leaves, roots, and stems are commonly prepared by boiling, and the resulting decoction is consumed for therapeutic purposes. *Talinum paniculatum*, known in Indonesia as Javanese Ginseng, shares characteristics with other well-known traditional medicinal plants, such as Panax Ginseng from East Asia (Oluba et al., 2019). Different studies have reported that Javanese Ginseng is rich in phytochemicals, including flavonoids, tannins, triterpenes, saponins, polyphenols, and polysaccharides (Aini and Susilo, 2023; Suriani et al., 2024). Furthermore, the Javanese ginseng plant also contains important sterol compounds such as campesterol, stigmasterol, and sitosterol as its main bioactive components (Tolouei et al., 2019). Pharmacologically, Javanese Ginseng is known to possess different biological activities, including antioxidant properties (Souto et al., 2021), free radical scavenging and anticancer activities (Aini and Susilo, 2023), potential in treating cardiovascular disorders, and strong antibacterial properties against *Candida albicans*, *Escherichia coli*, and *Staphylococcus aureus* (Tolouei et al., 2019). The root of Javanese ginseng (*Talinum paniculatum*) has also been reported to have hypoglycemic effects (Jenie and Indraswari, 2021). Therefore, a study on the use of Javanese ginseng (*Talinum paniculatum*), particularly its leaf decoction, is important to conduct in order to provide information on its hypoglycemic effects, as well as its influence on SOD levels and the histopathology of pancreatic tissue in diabetic rats. The present study aimed to evaluate the effects of a decoction of Javanese ginseng leaf simplicia (DJGLS) on blood glucose levels, SOD levels, and expression in the serum and pancreas of DM rats

MATERIALS AND METHODS

Ethical approval

All experimental procedures used in the study required approval from the Animal Research Ethics Committee, Faculty of Veterinary Medicine, Udayana University, Bali, Indonesia, which evaluated and approved the animal experiments. (Number: B/179/UN14.2.9/PT.01.04/2025)

Preparation of Javanese ginseng decoction

The preparation of decoction of Javanese ginseng leaf simplicia (DJGLS) was adapted from the method described by Jenie and Indraswari (2021). Fresh leaves of *Talinum paniculatum* (Javanese ginseng) were obtained from Dewandaru Flora Organic Farm, Tabanan Regency, Bali, Indonesia. The fresh green leaves were sorted and air-dried under morning sunlight between 08:00 and 10:00 until completely dried. The dried leaves were then ground using a blender (Type HR 2115, Philips, Indonesia) to obtain simplicia powder. A total of 100 g of the simplicia powder was mixed with 400 mL of distilled water and heated until the temperature reached 90°C, then maintained for 10 minutes. The resulting solution was filtered through a clean cotton cloth into a volumetric flask. Distilled water was subsequently added to the flask to obtain a final volume of 100 mL, resulting in a preparation equivalent to 100 g/100 mL (w/v) of simplicia powder. The mentioned preparation served as the stock solution of simplicia powder for administration to the experimental rats.

Phytochemical test

A total of 25 g of Javanese ginseng leaf powder was mixed with 500 mL of 80% ethanol and stirred gently, then allowed to stand for 24 hours, placed at room temperature, and wrapped with aluminum foil. The mixture was subsequently filtered using a clean cotton cloth to obtain the filtrate. The filtrate was then concentrated using a vacuum rotary evaporator (IKA RV 10, Germany) at 50°C until a thick extract was obtained. The resulting extract was subjected

to phytochemical screening to identify the presence of alkaloids, flavonoids, saponins, tannins, and steroids, following a method adapted from [Nortjie et al. \(2022\)](#).

Experimental preparation and treatment

Twenty adult male white rats of the Sprague-Dawley strain, weighing 135-140 g, were obtained from the Bio-Mice and Rat experimental animal breeding facility in Denpasar, Bali, Indonesia. The rats were housed individually in cage boxes (45 × 30 × 20 cm). The animal room was maintained at a temperature of 23-25°C. During a one-week acclimatization period, the rats were provided with pellet-form feed (Br II, Japfa Comfeed Tbk, Indonesia) and drinking water *ad libitum*. After the acclimatization period, the rats were randomly divided into four groups, including the GJ-0 group (n = 5), which served as the normal control, while the other three groups were DM rats, namely GJ-1 (n = 5), GJ-2 (n = 5), and GJ-3 (n = 5). Diabetes mellitus in rats was induced by a single dose of 1% streptozotocin (STZ, Sigma-Aldrich Inc., USA) solution (40 mg/kg body weight) dissolved in 50 mM sodium citrate buffer (pH 4.5; [Wu et al., 2021](#)), via intraperitoneal injection. Four days after injection, the rats were fasted for 12 hours, and blood glucose levels were measured using a glucometer (GlucoDr.™AGM-2100, allmedicus, Korea). Rats were considered diabetic when their blood glucose levels exceeded 200 mg/dL, according to [Furman \(2021\)](#). Afterward, rats in the GJ-0 and GJ-1 groups were administered a placebo (distilled water) at a volume of 1 mL/100 g body weight. Diabetic rats in the GJ-2 and GJ-3 groups were administered a decoction of Javanese ginseng leaves simplicia (DJGLS), prepared at a dose of 100 g/100 mL (w/v) with a volume of 0.5 mL and 1 mL per 100 g body weight per day, respectively. The treatments were given orally using gastric gavage for 21 consecutive days.

Sample collection

On day 22, the rats were deeply anesthetized with ketamine 40 mg/kg body weight and xylazine 5 mg/kg body weight (veterinary use only, Troy Laboratories PTY LTD, NSW, Australia) administered intramuscularly into the thigh muscle. Following confirmation of anesthesia, euthanasia was performed by cervical dislocation in accordance with the AVMA Guidelines for the Euthanasia of Animals ([AVMA, 2020](#)).

Blood samples were collected from the orbital vein using a hematocrit capillary tube and transferred into tubes without anticoagulant to obtain serum. The pancreas was carefully removed and divided into two portions. One portion was fixed in 10% neutral buffered formalin for the preparation of histopathological and immunohistochemical staining slides. The remaining portion was placed in a clean container and stored in a refrigerator at 4°C conditions for the determination of superoxide dismutase levels using an ELISA kit (Bioassay Technology Laboratory, Cat. No. E0168Ra, Zhejiang, China). ELISA analysis was performed on the same day (within a single day). Samples were collected in the morning, and the analysis was conducted in the afternoon. While awaiting preparation for the analysis, the samples were stored in a refrigerator.

Determination of blood glucose level

Blood glucose levels were determined using the blood glucose monitoring system GlucoDr.™AGM-2100 (allmedicus, Korea) according to [Jendrike et al. \(2017\)](#). Blood glucose measurements were performed on day 4 in both normal rats and STZ-injected rats. The data obtained from the measurement of glucose levels were used as the baseline blood glucose levels and were designated as day 0 for both normal and diabetic (DM) rats. Blood glucose levels were measured again at the end of the treatment period (day 22). Before measurement, the rats were fasted overnight (12 h) without access to food and water.

Determination of superoxide dismutase levels

The SOD levels were determined using an ELISA Kit (rat Superoxidase dismutase, Bioassay Technology Laboratory, China) using the procedure listed on the kit. The pancreatic tissue was rinsed in PBS (pH 7.4) to thoroughly remove excess blood and weighed prior to homogenization. The pancreas was minced and then placed into a 1.5 mL microtube containing PBS (pH 7.4). The sample was kept on ice in a beaker glass and subsequently sonicated for 1 minute using an ultrasonic homogenizer (Ultrasonicator, Tefic Biotech Co., Limited, China). The homogenate was centrifuged (Thermo scientific™ Multifuge, USA) at 2000-3000 rpm for approximately 20 minutes, and the supernatant was collected and transferred into an Eppendorf tube for immediate analysis. The plate was pre-coated with rat SOD antibody. The SOD present in the sample was then added and bound to the antibody coating the wells. Afterward, biotinylated rat SOD antibody was added and bound to the SOD in the sample. Streptavidin-HRP was then added and bound to the biotinylated SOD antibody. After incubation, unbound streptavidin-HRP was removed by washing. Substrate solution was then added, and color development was proportional to the amount of rat SOD in the sample. The

reaction was stopped by adding an acid stop solution, and absorbance was measured at 450 nm with an ELISA reader (Thermo Scientific Multiskan GO, Japan).

Histopathological staining

Histopathological staining was performed using hematoxylin and eosin (H&E) staining adapted from the method of Suarsana et al. (2020), which was originally applied to liver and kidney tissues. In the present study, pancreatic tissue was fixed in 10% neutral buffered formalin for 24h in room temperature, followed by dehydration, washing, paraffin embedding, and sectioning. Thin sections (4 μm) were floated on warm water, flattened, mounted onto glass slides, and allowed to dry. The sections were then stained with H&E solutions, dehydrated, rinsed, and mounted with a cover glass. Each slide was examined in five different fields of view. Observations were performed under a light microscope at 400x magnification equipped with a camera (Olympus CX33 microscope, Japan).

Immunohistochemical staining

The immunohistochemical analysis was performed using a procedure adapted from Magaki et al (2019). Five prepared slides from each group were subjected to immunohistochemical staining. The procedure was carried out as follows. Pancreatic tissues embedded in paraffin were sectioned at a thickness of 4 μm and mounted on silane-coated glass slides. The sections were then deparaffinized and rehydrated using standard protocols, followed by antigen retrieval. Endogenous peroxidase activity was blocked by immersing the slides in 3% hydrogen peroxide solution. To reduce nonspecific background staining, the sections were incubated with bovine serum albumin as a blocking serum. Subsequently, 200 μL of diluted primary antibody (1:200 dilution; SOD sc-101523; Santa Cruz Biotechnology, Oregon, USA) was applied to each slide and incubated at room temperature for 80 minutes. The slides were then incubated with a species-specific secondary antibody (Histofine Simple Stain MAX PO, Nichirei Biosciences Inc., Japan) for 15 minutes. After incubation, the slides were washed three times with 0.1% TBS-Tween solution. Chromogen development was performed by incubating the sections for 5 minutes, followed by rinsing in three changes of deionized water until the wash solution became clear. The sections were then counterstained with hematoxylin for 30 seconds and rinsed with several changes of distilled water. Subsequently, the slides were dehydrated, cleared in three changes of xylene, and mounted with a coverslip. Finally, the stained sections were examined under a light microscope (Olympus CX33 microscope, Japan).

Statistical analysis

The present study used a completely randomized design. Serum and pancreatic SOD levels were analyzed using One-Way ANOVA (Analysis of Variance). The significance level was set at 0.05, and to determine differences among treatment means, Duncan's Multiple Range Test was subsequently applied. While H&E staining and immunohistochemistry results were analyzed descriptively. The analysis was performed using SPSS version 26 software.

RESULTS

Phytochemical test

Phytochemical tests of Javanese ginseng (*Talinum paniculatum*) extract revealed the presence of different bioactive compounds. Qualitative test results indicated positive reactions for all tested parameters, namely alkaloid, flavonoid, saponin, tannin, and steroid (Table 1).

Blood glucose analysis

Blood glucose levels in rats differed markedly among the treatment groups. The normal group (GJ-0) revealed a mean blood glucose level of 119.6 mg/dL, whereas the diabetic group (GJ-1) of 400 mg/dL. At the end of the treatment period, the GJ-2 group exhibited a blood glucose level of 317.0 mg/dL, representing a reduction of approximately 42.1%, whereas the GJ-3 group indicated a level of 234.2 mg/dL, corresponding to a 51.4% decrease. Despite these reductions, blood glucose levels in both treatment groups remained higher than those observed in the normal control group (Table 2).

Serum analysis and pancreatic superoxide dismutase levels

The results of the analysis of SOD levels in the serum and SOD in the pancreas of diabetic rats treated with Javanese ginseng (*Talinum paniculatum*) extract are presented in Table 2. Serum SOD levels indicated in the GJ-0 treatment group were lower and significantly different ($P < 0.05$) compared to the GJ-1, GJ-2, and GJ-3 groups. The serum SOD level in the GJ-2 group (diabetic rats) treated with DJGLS at 50 g/100 mL was lower, but not significantly different ($P > 0.05$) compared to the GJ-1 group (diabetic rats). Meanwhile, in the GJ-3 group (diabetic rats) treated with DJGLS at 100 g/100 mL, the serum SOD level was lower and significantly different ($P < 0.05$) compared to the GJ-1 group (diabetic rats; Table 3).

Measurements of pancreatic SOD enzyme levels indicated that the diabetic group (GJ-1) had the lowest pancreatic SOD levels, significantly different ($P < 0.05$) compared to the other groups, indicating significant oxidative stress due to hyperglycemia. Conversely, DJGLS treatment in the GJ-2 and GJ-3 groups significantly increased ($P < 0.05$) pancreatic SOD levels compared to the GJ-1 group, but the levels were not significantly different ($P > 0.05$) compared to the normal control group (GJ-0). The increase in pancreatic SOD levels indicated that administration of DJGLS is quite effective in improving the endogenous antioxidant activity of SOD in the pancreatic tissue of diabetic rats, although the levels have not yet completely reached normal levels (Table 3).

Table 1. The phytochemical tests on Javanese ginseng extract ingredients

Parameter	Test type	Test results
Alkaloid	Wagner test	Positive
	Dragendorff's test	Positive
	Mayer's test	Positive
Flavonoid	Zinc and Magnesium test	Positive
Saponin	Foam saponin test	Positive
Tanin	Lead acetate test	Positive
Steroid	Lieberman test	Positive

Table 2. Blood glucose level in experimental rats of the Sprague-Dawley strain for 21 days of treatment

Groups	Adaptation period	Post STZ injection day 4 (baseline on day 0)**	After intervention (day 22)	Changes (%; from day 0-22)
GJ-0	109.8 ± 6.42 ^a	112.2 ± 4.71 ^a	119.6 ± 5.37 ^a	6.6 %
GJ-1	100.4 ± 3.36 ^a	502.2 ± 31.59 ^b	400 ± 22.47 ^b	20.4 %
GJ-2	102.6 ± 5.94 ^a	488.6 ± 46.90 ^b	317 ± 27.56 ^{bc}	42.1 %
GJ-3	103.4 ± 5.77 ^a	481.0 ± 58.01 ^b	234.2 ± 15.61 ^c	51.4 %

^{a,b,c} Different superscript letters in the same column indicate significant differences between treatments ($p < 0.05$). GJ-0: Normal control group, GJ-1: Diabetic group, GJ-2 and GJ-3: Diabetic group treated with decoction of Javanese ginseng leaf simplicia (DJGLS; 100g/100 mL) of 0.5 mL and 1 mL per 100 g body weight, respectively**. Post-STZ injection day 4 (used as the baseline on day 0 of the Javanese ginseng leaf decoction treatment). STZ: Streptozotocin.

Table 3. Average superoxide dismutase levels in serum and pancreas of diabetic rats of the Sprague-Dawley strain for 21 days of treatment

Group	Parameter	SOD serum		SOD pancreas	
		Concentration (ng/mL)*	Changes (%)	Concentration (ng/mL)*	Changes (%)
GJ-0		1.893 ± 0.254 ^a	-	2.404 ± 0.573 ^b	-
GJ-1		3.115 ± 0.326 ^b	64.5%	0.716 ± 0.284 ^a	(70.2%)
GJ-2		2.803 ± 0.408 ^{bc}	48.1%	2.031 ± 0.364 ^b	(15.5%)
GJ-3		2.476 ± 0.331 ^c	30.8%	2.215 ± 0.338 ^b	(7.9%)

^{a,b,c} Different superscript letters in the same column indicate significant differences between treatments ($p < 0.05$). GJ-0: Normal control group, GJ-1: Diabetic group, GJ-2 and GJ-3: Diabetic group treated with decoction of Javanese ginseng leaf simplicia (DJGLS; 100g/100 mL) of 0.5 mL and 1 mL per 100 g body weight, respectively. SOD: Superoxide dismutase. The data is presented as mean ± standard deviation.

Histopathological staining with hematoxylin and eosin

In H&E staining of the pancreas of the normal group (GJ-0), the microstructure of the pancreatic lobule is maintained, and the exocrine acini cells are neatly arranged with dense basophilic cell nuclei and eosinophilic cytoplasm. The islets of Langerhans appeared with relatively clear boundaries, compact islet cells, round/ovoid nuclei, and homogeneous nuclear cell distribution. H&E staining in GJ-1 indicated histopathological changes, the size of the islets of Langerhans was reduced (shrinking) with more fragile and heterogeneous islet cells; some beta cells indicated pyknotic nuclei and necrosis. H&E staining in GJ-2 indicated partial improvement in some islets of Langerhans, indicating recovery of the relative size and density of the islet cells, appearing more compact compared to the diabetic group (GJ-1). Signs of necrosis are reduced but not completely eliminated. H&E staining in GJ-3 indicated more marked improvement; the islets of Langerhans are clearer with cells indicating more intact nuclei and fewer pyknotic cells (Figure 1).

Superoxide dismutase immunohistochemical staining of the pancreas

The SOD immunohistochemical staining in GJ-0 indicated a strong positive reaction (intense brown color) to SOD expression, especially in the islet cells of Langerhans. The distribution of brown color appeared homogeneous in the cytoplasm of β cells. In some sections, there was a loss of positive staining. Immunohistochemical results in the GJ-2 group indicated a moderate increase in brown intensity compared to the diabetic group (GJ-1). Brown color appeared more pronounced in the cytoplasm of islet cells, although not as homogeneous as in a normal pancreas. Immunohistochemical results in the GJ-3 group indicated a fairly strong positive reaction (quite dark brown) that almost approached the condition of a normal pancreas. The distribution of color was more evenly distributed throughout the islet area (Figure 2).

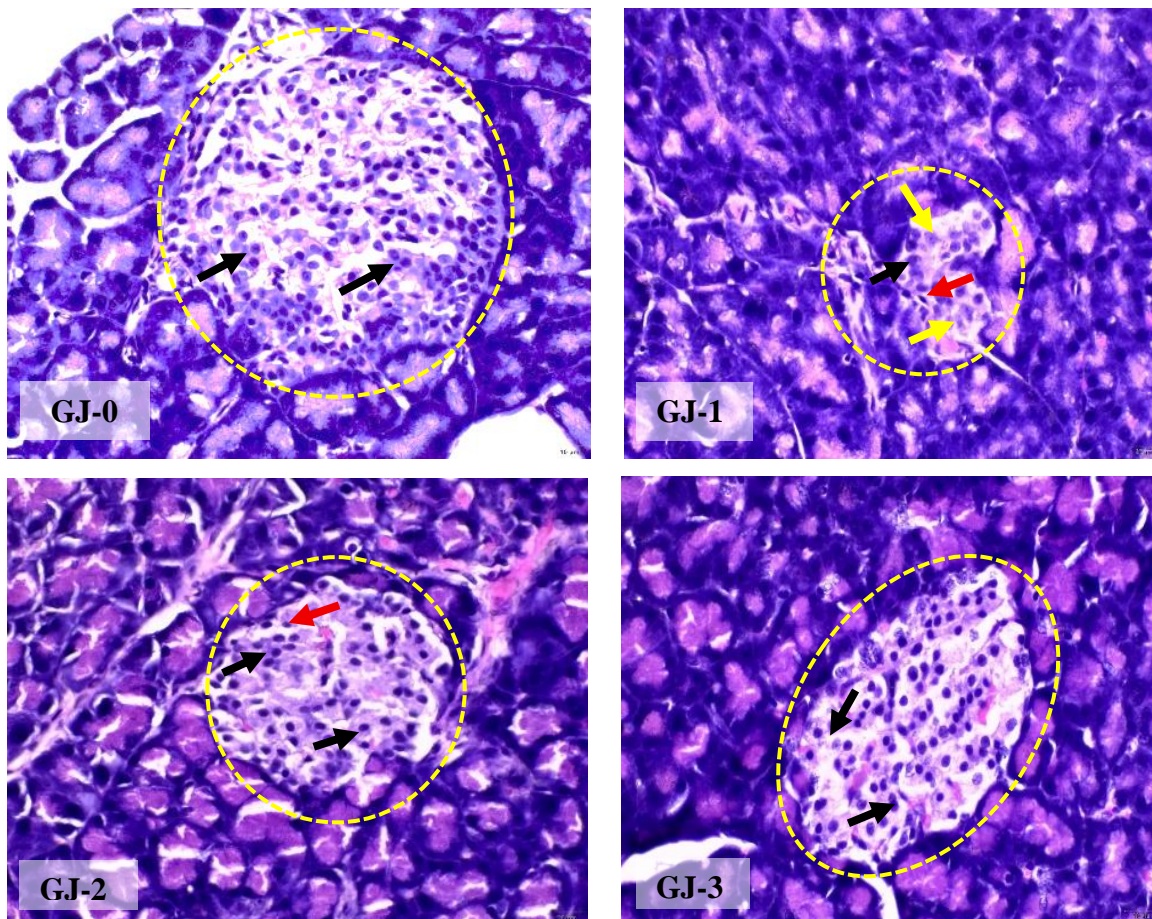


Figure 1. The H&E staining of pancreatic tissue of diabetic rats of the Sprague-Dawley strain after 21 days of treatment. **GJ-0:** Normal control group, **GJ-1:** Diabetic group, **GJ-2 and GJ-3:** Diabetic group treated with decoction of Javanese ginseng leaf simplicia (DJGLS; 100g/100 mL) of 0.5 mL and 1 mL per 100 g body weight, respectively. Islet cells are indicated by black arrows, necrosis is indicated by yellow arrows, pyknotic cell nuclei are indicated by red arrows, and yellow circles indicate islets of Langerhans. The scale bar is 10 μ m, and the magnification is 400x.

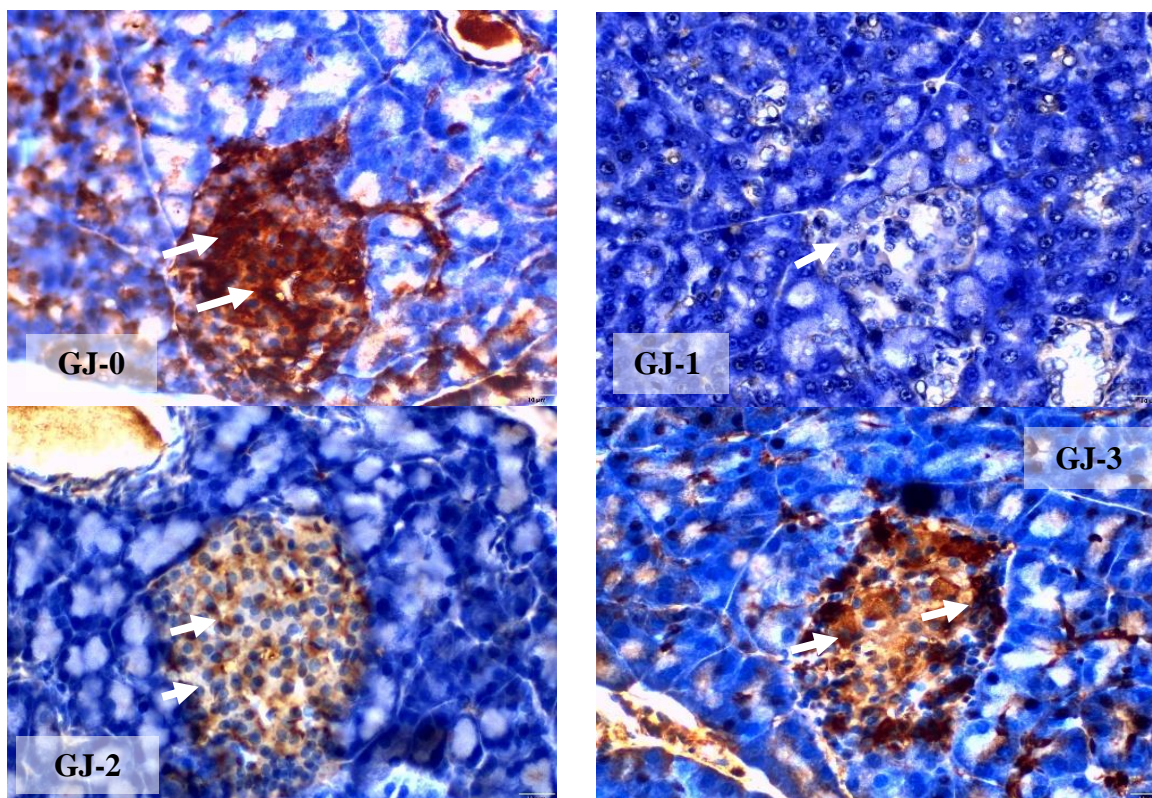


Figure 2. The Superoxide dismutase immunohistochemical staining of the pancreas in diabetic rats of the Sprague-Dawley strain for 21 days of treatment. **GJ-0:** Normal control group, **GJ-1:** Diabetic group, **GJ-2 and GJ-3:** Diabetic group treated with decoction of Javanese ginseng leaf simplicia (DJGLS; 100g/100 mL) of 0.5 mL and 1 mL per 100 g body weight, respectively. The scale bar is 10 μ m, and the magnification is 400x.

DISCUSSION

Medicinal plants are important sources of bioactive compounds and have long been widely utilized in traditional medicine. It is estimated that 70-90% of the global population relies on herbal remedies for healthcare, particularly in developing countries with high levels of biodiversity (Tran et al., 2020). The *Talinum paniculatum*, commonly known in Indonesia as Javanese ginseng, shares similarities with other well-known traditional medicinal plants, such as *Panax ginseng* in East Asia (Zheng et al., 2017; Park et al., 2021). In Indonesian traditional practices, different parts of the plant, including the leaves, roots, and bark, are commonly boiled and consumed as herbal preparations to treat several ailments (Susilo et al., 2024).

In this study, a decoction of Javanese ginseng (*Talinum paniculatum*) leaves was administered to streptozotocin (STZ)-induced diabetic rat models. Following STZ induction, rats in the GJ-1, GJ-2, and GJ-3 groups exhibited mean blood glucose levels exceeding 200 mg/dL, confirming the diabetic condition (Furman, 2021). Hyperglycemia in diabetic rats is generally defined by blood glucose levels ≥ 200 mg/dL. A study conducted by Qinna and Badwan (2015) reported that a single STZ dose of 80 mg/kg body weight can elevate blood glucose levels to 451-750 mg/dL. In the present study, rats injected with a single STZ dose of 40 mg/kg body weight indicated blood glucose levels ≥ 200 mg/dL by day 4. The mean glucose levels were 502.2 ± 31.59 mg/dL in the positive control group (GJ-1), 488.6 ± 46.90 mg/dL in the GJ-2 group, and 481.0 ± 58.01 mg/dL in the GJ-3 group. Blood glucose levels at the end of the treatment, particularly in the GJ-1 group (diabetic rats given a placebo, distilled water), decreased by 20.4% (from 502.2 to 400 mg/dL). In view of this, the decrease in blood glucose levels in diabetic rats (GJ-1 group) may be attributed to physiological adaptation (compensatory mechanisms).

The possibility of natural recovery cannot be completely excluded, since the untreated diabetic group (GJ-1) also indicated a 20.4% reduction in blood glucose levels during the 21-day study period. However, the reductions observed in the treatment groups, namely GJ-2 (42.1%) and especially GJ-3 (51.4%), were substantially greater than those in the untreated diabetic control group. The finding suggested that DJGLS treatment exerted an additional antihyperglycemic effect beyond the natural recovery process. Furthermore, the tendency for greater glucose reduction with increasing doses also supports the assumption that the decrease in blood glucose levels was associated with the therapeutic effect of DJGLS treatment rather than being solely due to natural recovery.

The reduction in blood glucose levels in diabetic rats may be attributed to physiological adaptation (body compensation) and the presence of compensatory β -cell mass expansion, primarily achieved through increased regeneration and proliferation of β -cells (Ackerman and Gannon, 2007). According to Kataoka et al. (2013), β -cell damage caused by streptozotocin (STZ) or alloxan is not always complete; β -cell mass gradually undergoes regeneration, allowing partial recovery of insulin function to reduce blood glucose levels, although glucose tolerance remains impaired. According to Gojani et al. (2024), β -cell regeneration is the process of restoring or increasing the number of functional pancreatic β -cells that produce insulin. The mentioned process can occur through natural physiological mechanisms involving two main pathways, including β -cell proliferation, in which existing β -cells divide to increase their number, and neogenesis from progenitor cells, in which pancreatic stem or progenitor cells differentiate into new β -cells (Gojani et al. 2024).

The study conducted by Jenie and Indraswari (2021) reported the use of Javanese ginseng root infusion given to alloxan-induced diabetic rats with a dose of 2% w/v solution with a volume of 1.8 mL/200 g body weight for 14 days, which significantly reduced blood glucose levels compared with untreated diabetic rats. Phytochemical analysis of the ethanol extracts of *Talinum paniculatum* leaves and roots identified 16 active compounds in the leaves and 17 in the roots, including phytol (a diterpenoid), stigmasterol (a steroid), and tocopherol (Susilo et al., 2024). The biological activity has been reported in international literature, and found that stigmasterol has been reported to possess antidiabetic properties (Wang et al., 2017), and tocopherol is also well known for its antioxidant effects (Liu et al., 2022). A study by Aini and Susilo (2023) on the bark extract of Javanese ginseng (*Talinum paniculatum*) identified 20 active compounds. The bark extract demonstrated significant anti-inflammatory activity and exhibited antioxidant potential.

Javanese ginseng (*Talinum paniculatum*) shared several characteristics with other well-known traditional medicinal plants, such as *Panax ginseng*, commonly known as Korean red ginseng (Zheng et al., 2017). Korean red ginseng has long been used in traditional medicine to help prevent and manage different diseases, including diabetes, cancer, inflammatory conditions, nervous system disorders, cardiovascular diseases, and hyperlipidemia (Park et al., 2021).

A plant from the same genus, *Talinum triangulare*, has been reported to exhibit hypoglycemic effects (Oluba et al., 2019). In Oluba et al. (2019) study, streptozotocin (STZ)-induced diabetic rats were administered a flavonoid extract of *Talinum triangulare* leaves at a dose of 10 mg/kg body weight for 21 days. Results presented in that study suggest that administration of a flavonoid extract of *Talinum triangulare* leaves for 21 days normalized STZ-induced hyperglycemia

and its associated dyslipidemia by a mechanism involving inhibition of α -amylase and HMG-CoA reductase activities, respectively, in rats.

Different studies have reported that ginseng contains a variety of bioactive compounds, including flavonoids, tannins, triterpenes, saponins, polyphenols, and polysaccharides (Aini and Susilo, 2023; Suriani *et al.*, 2024), as well as important sterol compounds such as campesterol, stigmasterol, and sitosterol (Tolouei *et al.*, 2019). Based on international literature, saponins have been reported to make an important contribution due to their hypoglycemic effects, including enhancing insulin secretion and improving insulin receptor sensitivity (Al-Ishaq *et al.*, 2019). Tannins act as protein-binding compounds that can slow intestinal glucose absorption (Jomova *et al.*, 2025). Steroids have been reported to possess anti-inflammatory and immunomodulatory properties (Yin *et al.*, 2024). In addition, flavonoids are known to inhibit the enzymes α -glucosidase and α -amylase, thereby reducing intestinal glucose absorption and stimulating insulin secretion from pancreatic β -cells (Wu *et al.*, 2025).

Different studies have reported that hyperglycemia in diabetes can trigger the excessive formation of free radicals, leading to cellular damage and increased activity of endogenous antioxidant enzymes as the body attempts to neutralize oxidative stress (Maritim *et al.*, 2003; Giacco and Brownlee, 2010). Javanese ginseng may help reduce oxidative stress through its bioactive compounds, such as saponins, flavonoids, and polyphenols, which are capable of scavenging and neutralizing free radicals (Rizqia *et al.*, 2023; Nyandoro *et al.*, 2025). In addition, *Talinum paniculatum* has been reported to possess antioxidant properties (Souto *et al.*, 2021) and free radical-scavenging activity (Liao *et al.*, 2015). A study conducted by Attele *et al.* (1999) reported that the use of *Panax ginseng* can improve antioxidant status and reduce biomarkers of oxidative stress in diabetic rat models.

Hyperglycemia in diabetes is known to induce oxidative stress through the excessive production of ROS (González *et al.*, 2023). Hyperglycemia in diabetes also increased levels of pro-inflammatory cytokines and chemokines, enhanced infiltration of immune cells, including macrophages, inflammatory cells, and granulocytes, and the development of local inflammation (Böni-Schnetzler and Meier, 2019). Persistent hyperglycemia exerts toxic effects on pancreatic β -cells, leading to apoptosis or necrosis (Kim *et al.*, 2005) and ultimately resulting in a reduction in β -cell mass and impaired β -cell function (Costes *et al.*, 2021). A study by Yin *et al.* (2024) reported that ginseng extract promotes pancreatic β -cell regeneration and protects β -cells from inflammatory damage, thereby helping to maintain β -cell mass and function and supporting the repair of pancreatic islet injury. In addition, Jenie and Indraswari (2021) demonstrated the hypoglycemic effect of Javanese ginseng in diabetic rats, which may reduce hyperglycemia as a major source of free radical generation. Furthermore, Riyana *et al.* (2022) reported that Javanese ginseng root extract increased SOD activity and reduced malondialdehyde levels in rats subjected to oxidative stress.

CONCLUSION

The results of this study indicated that administration of a decoction of Javanese ginseng leaf simplicia (DJGLS) for 21 days in diabetic rats reduced blood glucose and serum SOD levels, although these values had not fully returned to normal. Furthermore, the DJGLS indicated potential protective effects against damage to pancreatic β -cells in the islets of Langerhans and increased the intensity of SOD expression in the islets of Langerhans, although the increase had not yet reached the level observed in the normal control group. The present study utilized a decoction of Javanese ginseng leaf simplicia. It is recommended that future studies perform extraction using different solvents, followed by analysis of the active compound constituents present. In addition, pancreatic beta-cell damage should be quantified to obtain more accurate results in drawing conclusions regarding the protective effects against beta-cell damage, as well as measuring color intensity using quantitative image analysis or a scoring system. Furthermore, the mechanism of action of the active compounds in the decoction of Javanese ginseng leaf simplicia requires further investigation. Improvements in serum SOD levels, pancreatic SOD levels, and pancreatic histopathology following DJGLS administration suggest the presence of an oxidative protective mechanism that may help prevent cellular damage. However, the specific mechanisms by which the bioactive components of DJGLS influence serum SOD levels, pancreatic SOD levels, and SOD expression in pancreatic tissue remain unclear and require further investigation.

DECLARATIONS

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Authors' contributions

I Nyoman Suarsana, contributed to the design of the experiment, supervision, treatment, data analysis, and drafting of the manuscript. I Made Kardena, conducted the data collection, data analysis, and drafting of the article. Ni Luh Suriani and Dewa Ayu Swastini contributed to the creation and analysis of extracts, the drafting of the manuscript, and the drafting of the article. I Made Artika, supervised and validated the manuscript and article. All authors have read and approved the final edition of the manuscript.

Availability of data and materials

All data underlying the findings of the present study are presented within the article, and no supplementary datasets are provided.

Competing interests

The authors have not declared any conflict of interest.

Ethical considerations

The authors confirm that the present manuscript is original, free from plagiarism, and has not been published elsewhere. The authors also stated that no AI tools were used during the writing of this manuscript. All authors have reviewed the original content of the manuscript.

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