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Effect of Purple Leaf (*Graptophyllum pictum* (L.) Griff) Emulsion on the Histological Parameters of Streptozotocin-Induced Diabetic Rats

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Abstract: Damage to vital organs such as the liver, kidneys, and pancreas is a common complication of diabetes mellitus, characterized by chronic hyperglycemia due to pancreatic cell dysfunction. *Graptophyllum pictum* (purple leaf) is a potential herbal therapy containing bioactive compounds with antioxidant and organ-protective effects. This study aimed to evaluate the effect of purple leaf emulsion on blood glucose levels and the histopathological features of diabetic rats induced by streptozotocin. Rats were divided into six groups: normal control, negative control, positive control (glibenclamide), and three doses of purple leaf emulsion (100, 200, and 300 mg/kg BW). After 28 days of treatment, the emulsion significantly reduced blood glucose levels and improved the histological structures of the liver, kidneys, and pancreas. The 200 mg/kg BW dose was most effective for pancreatic protection, while 300 mg/kg BW provided optimal hepatoprotective and renoprotective effects. These findings highlight the potential of purple leaf as a natural antidiabetic and organ-protective agent.

Keywords: Diabetes mellitus; *Graptophyllum pictum*; Kidney; Liver; Pancreas

Introduction

Type 2 Diabetes Mellitus (T2DM) is a complex chronic metabolic disease that is not only characterized by persistent hyperglycemia but also triggers microvascular and macrovascular complications that seriously impact vital organs, including the pancreas, liver, and kidneys. These complications significantly impair physiological function and contribute to an increase in global morbidity and mortality, with T2DM reported to be the cause of 26.8% of patient deaths (Antar et al., 2023; Zheng et al., 2018; Gieroba et al., 2025). In the kidneys, chronic hyperglycemia provokes diabetic nephropathy through various pathological mechanisms, such as increased oxidative stress, polyol pathway activation, formation of advanced glycation end products (AGEs), and protein kinase C activation. All these mechanisms lead to progressive vascular endothelial damage, which can ultimately result in kidney failure. Meanwhile, in the liver, diabetes can cause fat accumulation, inflammation, and hepatocyte necrosis, which are characteristic features of non-alcoholic fatty liver disease (NAFLD). NAFLD can arise both as a direct complication of T2DM and as a progressive risk factor for other vascular complications (Alalwani et al., 2022; Wu et al., 2023; Mir et al., 2025).

Pancreatic cells, particularly β-cells, are highly susceptible to oxidative stress due to their intrinsically low levels of antioxidant enzymes. Hyperglycemia increases the production of reactive oxygen species

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(ROS), which subsequently impairs insulin secretion, triggers mitochondrial dysfunction, and induces β-cell apoptosis. One of the key regulators in this process is thioredoxin-interacting protein (TXNIP), whose expression is elevated in prediabetic and T2DM conditions and is known to promote β-cell death (Młynarska et al., 2025; Gerber & Rutter, 2016; Bhatti et al., 2022). Moreover, unhealthy lifestyle factors such as central obesity, dyslipidemia, smoking, and physical inactivity are known to exacerbate metabolic dysregulation and accelerate the onset of complications in the kidneys, liver, and peripheral nerves (Geng et al., 2023; Vajdi et al., 2023; Meriana & Handayani, 2025; Vetter et al., 2018). T2DM is not merely a glycemic disorder but a multisystemic condition that exerts destructive effects on vital organs, predominantly through mechanisms involving oxidative stress.

Conventional DM therapy includes pharmacological agents and lifestyle modifications. However, the limitations and potential side effects of existing therapies encourage the search for alternative or complementary therapies. In this context, herbal plants have long been used in traditional medicine and are now attracting attention in modern research due to their bioactive compound content. Many herbal plants show potential antidiabetic effects through mechanisms such as increasing insulin secretion, improving insulin sensitivity, or inhibition of glucose absorption. One promising plant is the purple leaf (Graptophyllum pictum). Traditionally, purple leaf has been used for various health conditions, and phytochemical studies identify it as rich in bioactive compounds such as flavonoids, tannins, saponins, and alkaloids, which are known to have various pharmacological activities, including antioxidant and anti-inflammatory properties relevant to DM pathophysiology. Preliminary research also shows that purple leaf has the potential to affect glucose metabolism (Fajrianti et al., 2024; Priyanto et al., 2024; Kusumaningsih et al., 2018).

Purple leaf emulsion was used in this study. An emulsion can increase the solubility and bioavailability of lipophilic compounds found in purple leaf, thereby potentially increasing absorption and producing optimal therapeutic effects. In addition, an emulsion can increase the stability of active compounds against degradation and ensure better homogeneity and dose accuracy. Emulsion systems have been shown to increase the efficiency of encapsulation and oral absorption of active substances, while protecting bioactive content from gastrointestinal degradation, thereby increasing the bioavailability and therapeutic effects of herbal preparations (Li et al., 2022; Lim et al., 2023). This emulsion formulation approach is expected to maximize the antidiabetic potential of purple leaf. This study aims to evaluate the effect of purple leaf emulsion administration on blood glucose levels and histopathological features of the pancreas, liver, and kidneys in a diabetic animal model.

Method

Emulsion Preparation and Components

Emulsion preparation was carried out by adding purple leaf ethanol extract into an emulsion base, which was a mixture of Tween 80, Span 80, propylene glycol, Virgin Coconut Oil (VCO) as the oil phase, and distilled water as the aqueous phase. For the 100 mg/kg BW dose, 0.8 grams of extract were used; for the 200 mg/kg BW dose, 1.6 grams; and for the 300 mg/kg BW dose, 2.4 grams. Each was added to 100 mL of the emulsion base, then mixed homogeneously to form a stable emulsion preparation.

Phytochemical Test

The flavonoid test was performed by reacting 0.5 mL of emulsion with 10 mL of distilled water, heated in a water bath, filtered, then 1 mL of 96% ethanol, magnesium powder, and 10 mL of concentrated HCl were added. A positive result was indicated by an orange-red color for flavonoids.

The alkaloid test was performed by adding 5 mL of 2N HCl to 0.5 mL of emulsion, heating for 2 minutes, then 3 drops of Dragendorff's reagent were added. An orange yellow to brick-red precipitate indicated the presence of alkaloids.

The saponin test was performed by mixing 0.5 mL of emulsion with 10 mL of warm water and shaking vigorously for 10 seconds. The formation of stable foam for ≥1 minute or its not disappearing after the addition of 1 drop of 2N HCl indicated the presence of saponins.

The tannin test was performed by adding 20 mL of hot water and 3 drops of 10% NaCl solution to 0.5 mL of emulsion, then $FeCl_3$ solution was added. A bluish-black or greenish-black color indicated a positive result for tannins.

The steroid and terpenoid test was performed by mixing 0.5 mL of emulsion with 2 drops of anhydrous acetic acid and 1 drop of concentrated H_2SO_4. A color change to green indicated the presence of steroids, while a bluish-green color indicated the presence of terpenoid compounds.

Research Procedure

The method used was a laboratory experimental design with a pre-test and post-test randomized controlled group design. A total of 30 male Wistar strain rats (*Rattus norvegicus*) were randomly divided into six equal-sized groups with equal numbers. Three control groups: normal control given emulsion base without streptozotocin (STZ) induction, negative control

induced with STZ and given emulsion base, and positive control induced with STZ and given glibenclamide. Three treatment groups were induced with STZ and each given purple leaf emulsion at doses of 100 mg/kg BW, 200 mg/kg BW, and 300 mg/kg BW.

On day 0, the rats' blood glucose levels were measured as initial blood glucose levels, and they were then randomly divided into 6 groups. All groups, except the normal control, were induced with streptozotocin (40 mg/kg BW). On day 7, glucose levels were measured to confirm hyperglycemia, and then the rats were treated according to the group. Treatment was given orally for 21 days. Blood glucose levels were measured again on days 14, 21, and 28. On day 28, the rats were sacrificed, and the pancreas, liver, and kidney organs were taken for histopathological examination.

Blood glucose level measurement was performed using a digital strip glucometer, which allowed for rapid capillary glucose examination from the rat's tail. For histopathological analysis of the kidney, liver, and pancreatic organs, tissue preparations that had been fixed and stained using Hematoxylin-Eosin (H&E) staining were observed under a light microscope. Observations were made at 400x magnification and taken from 5 representative fields of view for each sample. The microscope used was a Pro Histo Biological Microscope Pro 31W, equipped with objective lenses and a lighting system suitable for detailed tissue morphological analysis.

Hematoxylin and Eosin (H&E) staining is a versatile technique used for formalin-fixed tissues. In this method, basophilic components like the nucleus stain blue, while acidophilic components such as the cytoplasm and extracellular matrix appear pink. This creates a clear contrast between the cell nucleus and the cytoplasm. For over a century, H&E has been the most used standard staining technique in histopathological analysis. Its widespread use across various tissue types is due to its compatibility and ability to highlight cellular morphology while detecting a broad range of lesion types, including degeneration, necrosis, and infiltration. H&E is routinely applied to many anatomical tissues, including the spleen, liver, kidneys, and pancreas (Maynard et al., 2023; Tanabe et al., 2025; Wick, 2019).

Observation of H&E staining results, whether viewed directly under a microscope or through digital slides, enables observations up to the cellular and subcellular levels, typically at 400x magnification or higher. Light microscopes are a common tool in tissue morphology analysis because of their ability to display cellular structures with contrast at high magnifications (Rieger et al., 2021).

Data Analysis

Blood glucose data and histopathological scores of tissue damage were statistically analyzed. A normality test was performed with the Shapiro-Wilk test, and a homogeneity test with the Levene test. Data were analyzed using the Kruskal-Wallis test, followed by the Mann-Whitney test between groups. Significance was set at $p<0.05$. Analysis was performed using SPSS version 25.

Research Location

This research was conducted at the Pharmaceutics and Pharmaceutical Technology Laboratory, Phytochemistry-Pharmacognosy Laboratory, and Biopharmaceutics Laboratory of STIFA Pelita Mas Palu. Histopathological sample preparation of the pancreas, liver, and kidneys was carried out at the Biopath Laboratory, Bandung.

Ethical Approval

This research has received ethical approval from the Medical and Health Research Ethics Committee of the Faculty of Medicine, Tadulako University (Approval number: 364/UN28.10/KL/2024).

Result and Discussion

Phytochemical analysis results were consistent with previous studies reporting that *Graptophyllum pictum* contains various secondary metabolites such as alkaloids, flavonoids, tannins, saponins, and steroids, which contribute to its pharmacological effects including antioxidant, antidiabetic, anti-inflammatory, and cytotoxic activities against liver and breast cancer cells (Tampang et al., 2024; Wardani et al., 2024). The high antioxidant activity of the ethanolic extract of purple leaf is supported by its elevated total phenolic and flavonoid content, which is capable of scavenging free radicals and reducing oxidative stress (Fajrianti et al., 2024; Makkiyah et al., 2024). The presence of these bioactive compounds has also been shown in vivo to reduce blood glucose levels and protect vital organs such as the liver, kidneys, and pancreas through α-glucosidase inhibition and enhancement of endogenous antioxidant activity (Priyanto et al., 2024; Unuofin & Lebelo, 2020). Administration of the ethanolic extract of purple leaf at higher doses demonstrated low toxicity and did not cause significant alterations in the hematological profiles of rats, confirming its potential as a relatively safe therapeutic agent. The results of the phytochemical screening test are presented in Table 1 (Dewi et al., 2024).

Streptozotocin (STZ) is a diabetogenic agent that selectively targets and damages pancreatic β-cells

through mechanisms involving oxidative stress and DNA damage, leading to decreased insulin levels and the induction of hyperglycemia. STZ enters β-cells via the GLUT2 transporter and causes specific cellular necrosis, making it the preferred compound for establishing experimental models of diabetes mellitus. The reduction in insulin levels resulting from pancreatic β-cell destruction impairs glucose uptake by peripheral tissues, ultimately leading to elevated blood glucose levels (hyperglycemia) and contributing to various organ complications (Gobinath et al., 2022; Mahata et al., 2021; Tana et al., 2024; Carnethon et al., 2012).

Table 1. Phytochemical Screening Results of *Graptophyllum pictum* (L.) Griff. Leaf Emulsion

Test	Reagents	Result	Description
Alkaloid	Dragendorff's reagent	Orange precipitate formed	+
Flavonoid	Magnesium powder and concentrated HCl	Orange color appeared	+
Saponin	Shaken with warm water + 2N HCl	Foam formed and persisted for 1 minute	+
Tannin	Addition of $FeCl_3$ solution	Dark green color appeared	+
Steroid	Acetic anhydride + concentrated H_2SO_4	Green color appeared	+

Note: (+) Contains tested compound, (-) Does not contain tested compound.

A decrease in blood glucose levels were observed after diabetic rats were induced with streptozotocin (STZ) and were treated for 21 days with purple leaf emulsion. The measurement on day 28, as presented in Table 2, showed that administration of the purple leaf emulsion significantly reduced blood glucose levels compared to the negative control group. The highest percentage reduction in blood glucose was recorded in the 200 mg/kg BW group (87.02%), followed by the 100 mg/kg BW group (84.3%) and the 300 mg/kg BW group (81.3%).

Statistical analysis using the Kruskal–Wallis test showed a significant difference in blood glucose levels among the groups ($p = 0.008$, $p < 0.05$). The post hoc Mann–Whitney test revealed that administration of the purple leaf emulsion at doses of 100, 200, and 300 mg/kg BW significantly differed from the negative control group, while no significant difference was observed compared to the normal and positive control groups. Based on these results, the purple leaf emulsion demonstrated a significant antihyperglycemic activity, with the most optimal effect observed at a dose of 200 mg/kg BW.

Table 2. Blood Glucose Levels of Rats

	Mean ± SD Blood Glucose Levels (mg/dL)						
Day	Normal control	Negative control	Positive control	Emulsion Dose 100 mg/kgBW	Emulsion Dose 200 mg/kgBW	Emulsion Dose 300 mg/kgBW	p value
0	81.6 ± 7.701	80.6 ± 17.053	89.2 ± 8.468	87.4 ± 12.818	80.8 ± 8.228	96.4 ± 19.527	0.360
7	84.8 ± 7.855	425.8 ± 6.419	438.2 ± 29.201	417.0 ± 9.247	437.2 ± 26.013	427.0 ± 8.093	0.012
14	77.6 ± 11.149	415.6 ± 7.765	109.2 ± 8.408	104.4 ± 15.010	116.4 ± 5.941	117.4 ± 16.288	0.001
21	77.4 ± 12.239	394.4 ± 39.690	88.8 ± 7.662	81.2 ± 7.596	85.4 ± 9.209	87.4 ± 7.570	0.010
28	75.6 ± 6.877	398.6 ± 20.107	72.8 ± 3.114	65.6 ± 19.398	65.6 ± 19.731	79.8 ± 4.658	0.008

Note: $p<0.05$ indicates a significant difference between groups, $p>0.05$ indicates no significant difference between groups

The improvement in blood glucose levels observed in the treatment groups was consistent with the histopathological findings of the pancreas, which showed clear differences between the purple leaf emulsion–treated groups and the negative control. Rats receiving the purple leaf emulsion exhibited lower tissue damage scores, characterized by reduced necrosis, cellular degeneration, and inflammatory cell infiltration compared to the negative control group. Necrosis is an uncontrolled form of cell death, typically caused by physical injury or exposure to toxic agents. This process is characterized by cellular swelling, rupture of the plasma membrane, and the release of intracellular contents that trigger an inflammatory response (Park et al., 2023; Rad et al., 2022; Hamdin et al., 2019). Prior to reaching this terminal stage, affected cells often exhibit degenerative changes such as swelling and vacuolization. The associated inflammation recruits immune cells, including monocytes and macrophages, to the site of injury. If this chronic inflammatory response persists, it can ultimately lead to fibrosis formation (Antar et al., 2023).

The statistical analysis using the Kruskal–Wallis test revealed a significant difference among the groups ($p < 0.05$). The highest mean score of pancreatic tissue damage was observed in the negative control group (1.16 ± 0.330), while the lowest score was found in the group treated with purple leaf emulsion at a dose of 200 mg/kg BW (0.42 ± 0.200), followed by the positive control group (0.49 ± 0.452), the 300 mg/kg BW group (0.51 ± 0.331), the normal control group (0.60 ± 0.538), and the 100 mg/kg BW group (0.93 ± 0.185). The Mann–

Whitney post hoc test indicated that the 100 mg/kg BW group differed significantly from the positive, negative, and normal control groups. In contrast, the 200 and 300 mg/kg BW groups showed significant differences compared to the negative control but not to the normal or positive control groups.

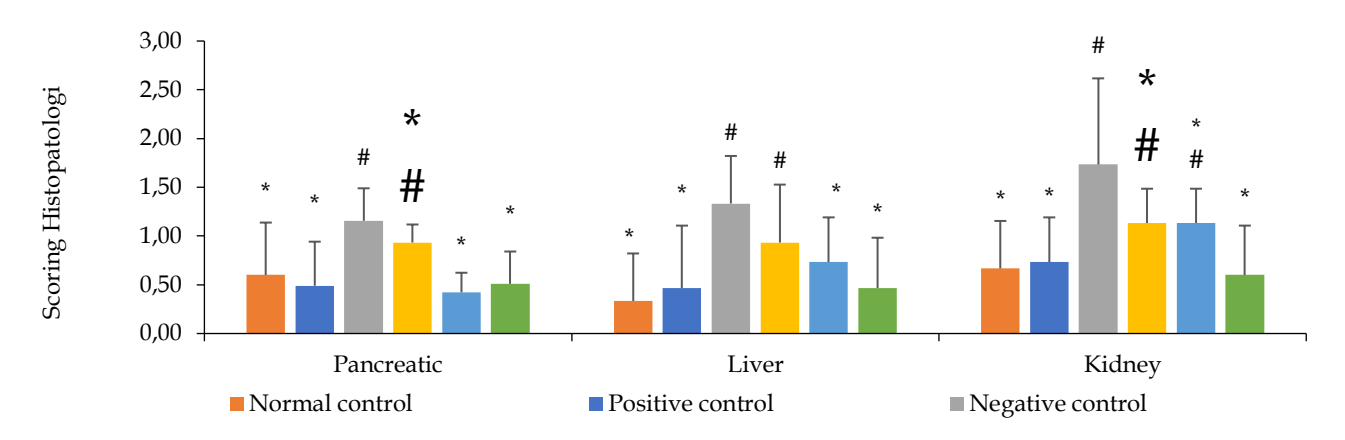

Figure 1. Mean ± standard deviation (SD) of histopathological scores. Asterisk (*) indicates a significant difference compared to the negative control group ($p < 0.05$); hash () indicates a significant difference compared to the positive control group ($p < 0.05$). The normal control group was used as a reference to describe the healthy tissue condition without treatment

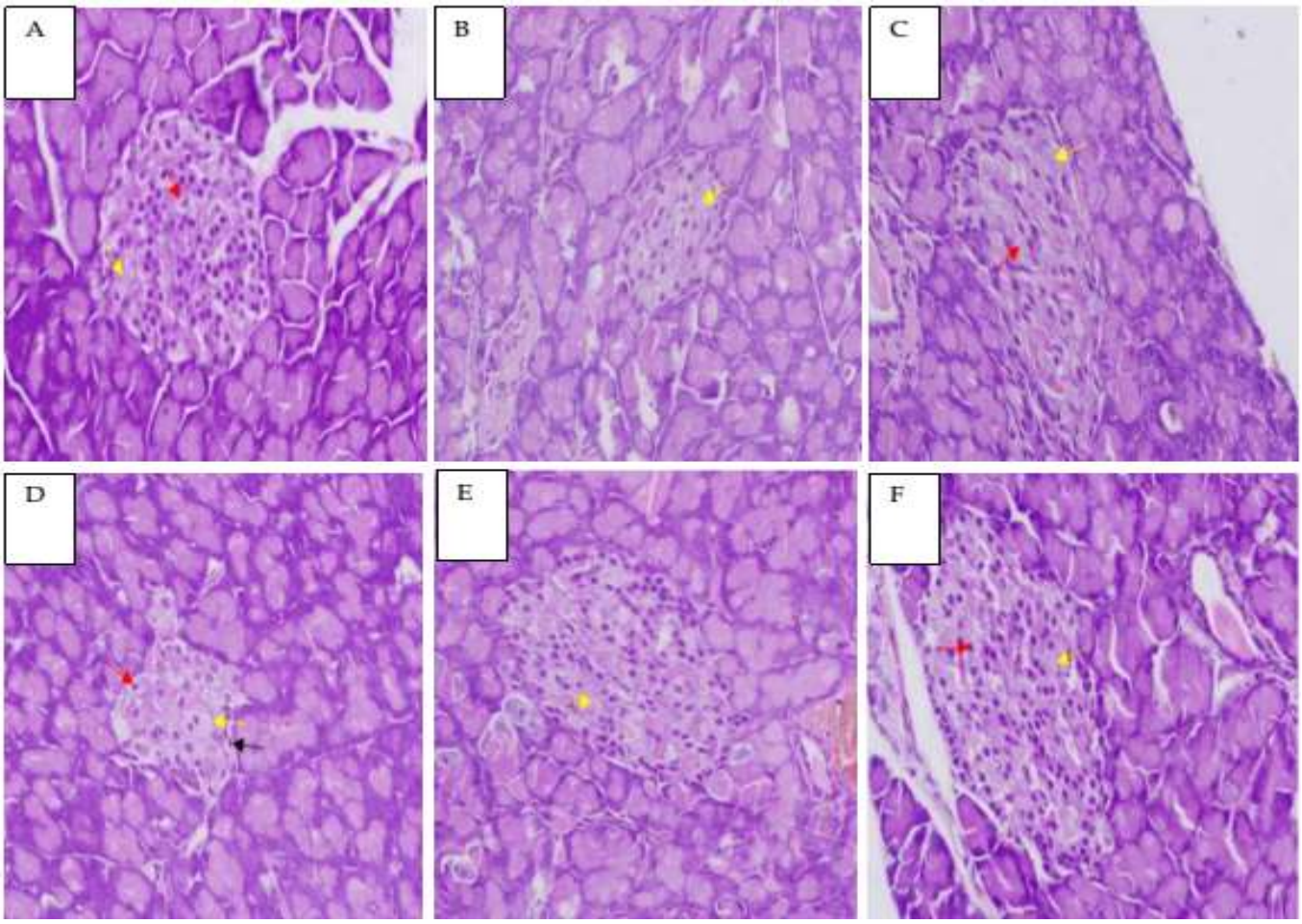

Figure 2. Pancreatic histopathology at 400x magnification with Hematoxylin and Eosin (HE) staining. A: normal control, B: positive control, C: negative control, D: 100 mg/kg BW dose, E: 200 mg/kg BW dose, and F: 300 mg/kg BW dose. The yellow arrow indicates necrosis, red indicates degeneration, and black indicates inflammatory cells

In addition to the pancreas, STZ induction is known to cause damage to both the liver and kidneys. In the liver, hyperglycemia triggers insulin resistance, which subsequently enhances lipolysis and leads to the accumulation of free fatty acids. The excessive buildup of these fatty acids promotes oxidative stress and inflammation through activation of the NF-κB signaling pathway and increased production of reactive oxygen species (ROS). Collectively, these processes contribute to hepatocyte degeneration, sinusoidal dilation, and other structural alterations within the hepatic tissue (Mahata et al., 2021; Robers et al., 2024; Tana et al., 2024). Histopathological analysis of the liver revealed that the negative control group exhibited the highest mean damage score (1.33 ± 0.488), whereas the group treated with the purple leaf's emulsion at a dose of 300 mg/kg BW showed the lowest score (0.47 ± 0.516). The mean scores for the 100 mg/kg BW and 200 mg/kg BW groups were 0.93 ± 0.594 and 0.73 ± 0.458, respectively, which were comparable to the positive control (0.47 ± 0.640) and slightly higher than the normal control (0.33 ± 0.488). Statistical analysis using the Kruskal–Wallis test indicated a significant difference among groups ($p < 0.05$). Post hoc Mann–Whitney analysis showed that the 100 mg/kg BW group differed significantly from the normal and positive controls but not from the negative control. The 200 and 300 mg/kg BW groups showed significant differences from the negative control, with no significant difference compared to the normal and positive controls.

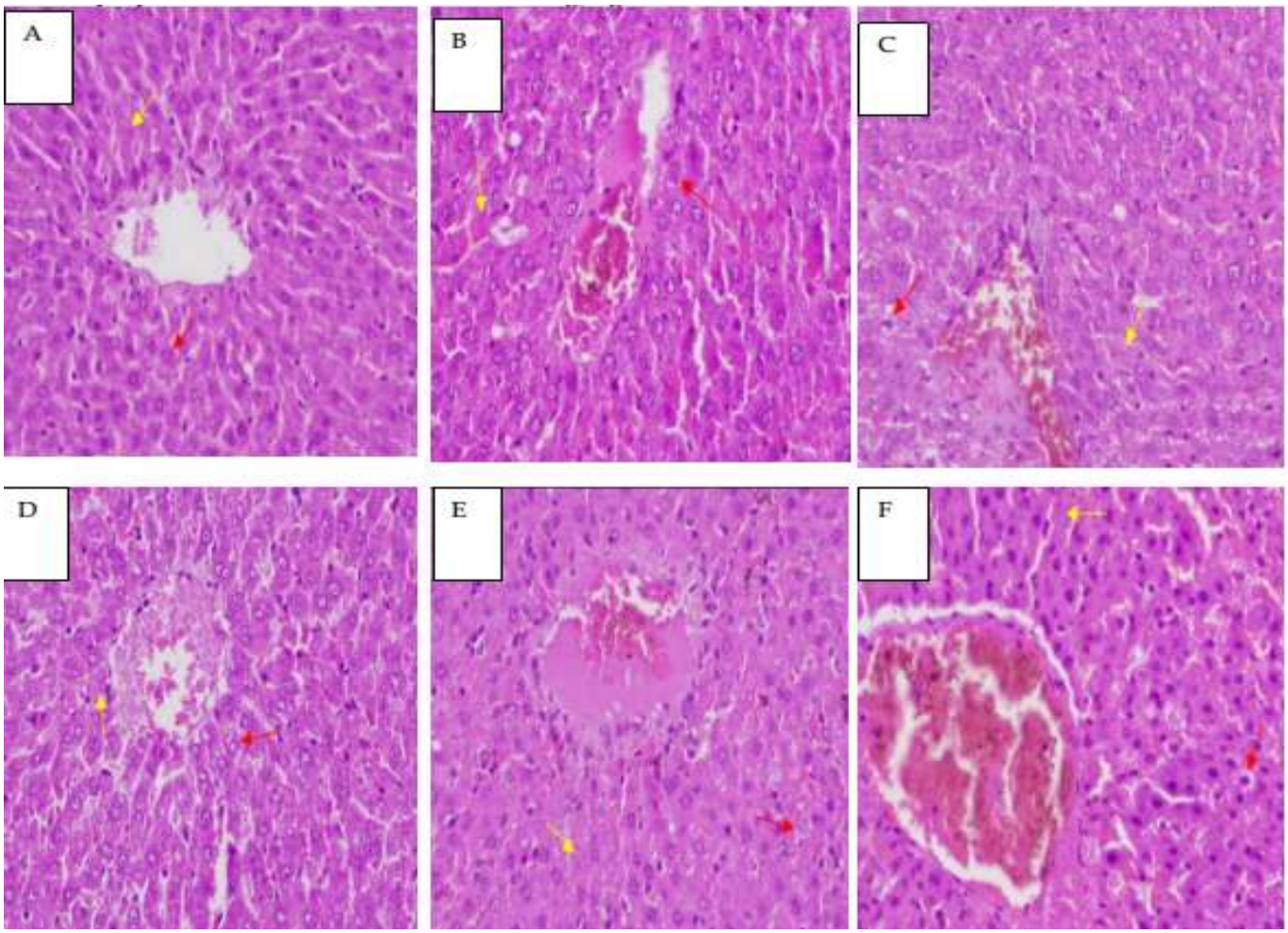

Figure 3. Liver histopathology at 400x magnification with Hematoxylin and Eosin (HE) stain-ing. A: normal control, B: positive control, C: negative control, D: 100 mg/kg BW dose, E: 200 mg/kg BW dose, and F: 300 mg/kg BW dose. The yellow arrow indicates necrosis, red indicates degeneration, and black indicates inflammatory cells

In the kidneys, STZ triggers diabetic nephropathy through increased expression of abnormal angiogenesis mediators such as leucine-rich α-2-glycoprotein-1 (LRG1), transforming growth factor-β1 (TGF-β1), activin-like kinase 1 (ALK1), and vascular endothelial growth factor (VEGF). Activation of this pathway leads to glomerular hypertrophy, Bowman's capsule widening, basement membrane thickening, and mesangial matrix accumulation, all of which are characteristics of progressive diabetic nephropathy. STZ

induction not only produces hyperglycemic conditions as a diabetes model but also triggers multiorgan damage resembling clinical DM complications in humans (Mohammad et al., 2023).

Histopathological analysis of the kidney showed that the negative control group had the highest mean damage score (1.73 ± 0.884), followed by the 100 mg/kg BW (1.13 ± 0.352) and 200 mg/kg BW (1.13 ± 0.352) groups. The lowest score was observed in the 300 mg/kg BW group (0.60 ± 0.507), which was comparable to the normal control (0.67 ± 0.488) and slightly lower than the positive control (0.73 ± 0.458). Statistical analysis using the Kruskal–Wallis test indicated a significant difference among groups ($p < 0.05$). Post hoc Mann–Whitney analysis revealed that the 100 mg/kg BW and 200 mg/kg BW groups differed significantly from the normal, positive, and negative controls, whereas the 300 mg/kg BW group differed significantly from the negative control but not from the normal or positive controls.

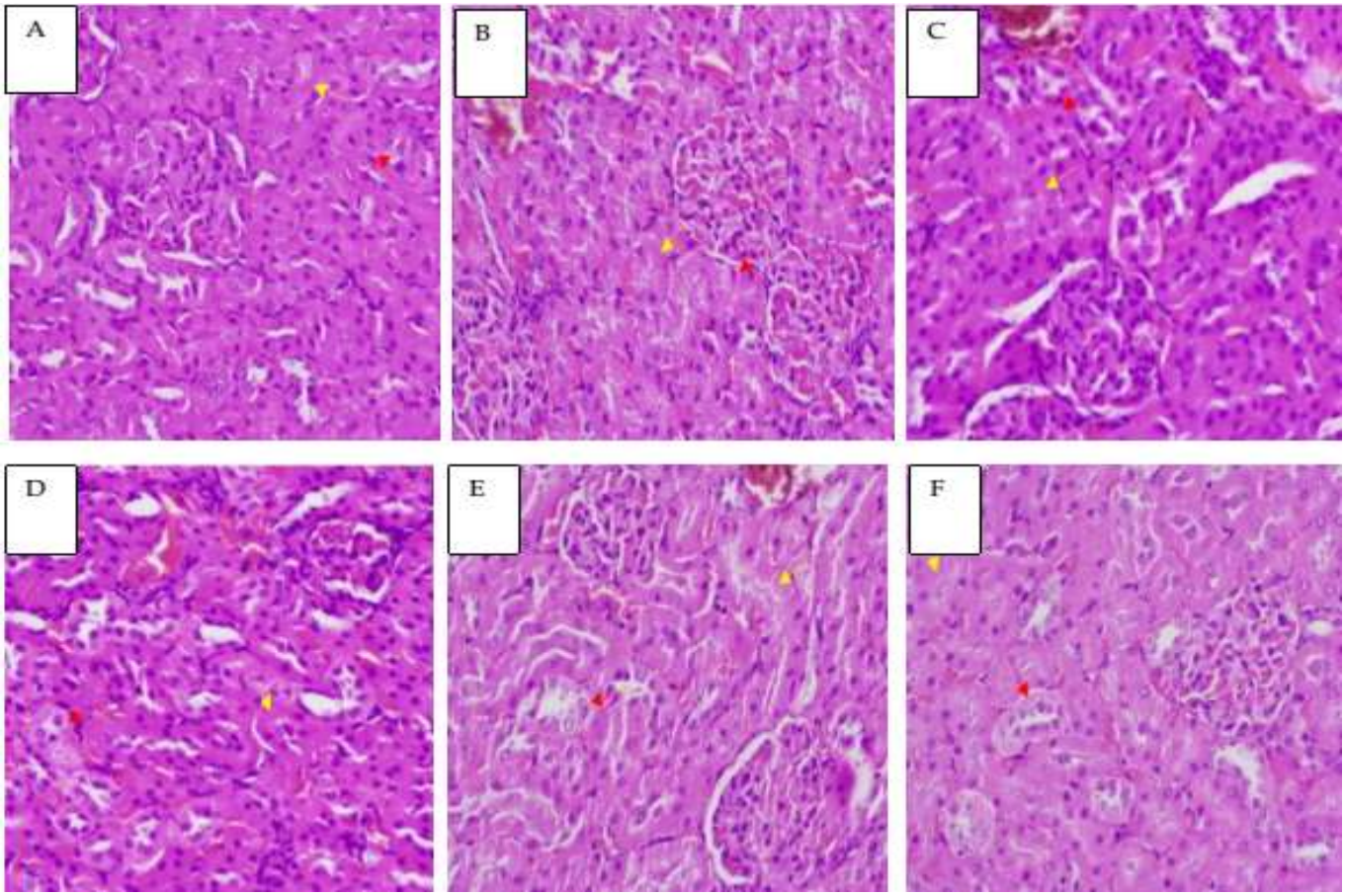

Figure 4. Kidney histopathology at 400x magnification with Hematoxylin and Eosin (HE) staining. A: normal control, B: positive control, C: negative control, D: 100 mg/kg BW dose, E: 200 mg/kg BW dose, and F: 300 mg/kg BW dose. The yellow arrow indicates necrosis, red indicates degeneration, and black indicates inflammatory cells

The administration of purple leaf emulsion exerted protective effects on vital organs compromised by diabetes mellitus, including the pancreas, liver, and kidneys. This organoprotective effect is primarily attributed to the presence of bioactive secondary metabolites, such as flavonoids, alkaloids, phenolics, and saponins, which confer antioxidant, anti-inflammatory, and anti-apoptotic activities (Darmayanti et al., 2024; Ocvinta et al., 2024). Alkaloids, in particular, exhibit pronounced anti-inflammatory properties that preserve tissue integrity and attenuate the progression of organ damage under chronic hyperglycemic conditions (Nie et al., 2024). Alkaloids mitigate tubular injury and fibrosis, largely through modulation of the TGF-β1 signaling pathway via upregulation of inhibitory proteins such as Smad7, thereby delaying the advancement of diabetic nephropathy (Mahmoud et al., 2021). Secondary metabolites from other medicinal plants have also been shown to enhance endogenous antioxidant defenses, promote insulin secretion, and suppress inflammation and apoptosis in pancreatic and hepatic tissues. Moreover, administration of plant extracts enriched in bioactive compounds has been associated with significant reductions in ALT, AST, ALP, urea, and creatinine levels, alongside improvements in the histological architecture of the

pancreas and kidneys. These findings are consistent with phytochemical analyses revealing the presence of flavonoids, alkaloids, and terpenoids, which are implicated in both antihyperglycemic activity and organ-protective effects (Woldekidan et al., 2021). Additionally, these metabolites demonstrate inhibitory activity against key glucose-metabolizing enzymes, including α-glucosidase and ATP citrate lyase, further substantiating their mechanistic basis as therapeutic agents in mitigating organ dysfunction associated with diabetes mellitus (Arshad et al., 2022).

Conclusion

Purple leaf emulsion significantly reduces blood glucose levels and demonstrates protective effects on pancreatic, hepatic, and renal tissues. The 200 mg/kg BW dose showed a greater reduction in blood glucose levels and pancreatic damage score, while the 300 mg/kg BW dose was optimal in protecting the liver and kidneys.

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Conflicts of Interest
The authors declare no conflict of interest.

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