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Innovative Oil from STIFA Pelita Mas for Glycemic Control and Tissue Regeneration in Diabetic Rats

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ABSTRACT

Introduction: Diabetes mellitus is a significant global health problem with increasing prevalence in Indonesia. Conventional management of diabetes mellitus is often accompanied by side effects and high costs, prompting the search for alternatives based on natural ingredients. STIFA Pelita Mas Herbal Oil is an innovative formulation that combines various efficacious natural ingredients, but its effectiveness on histopathological changes in pancreatic and kidney tissues due to diabetes has not been comprehensively explored. This study aims to evaluate the effectiveness and mechanism of action of STIFA Pelita Mas Herbal Oil on reducing blood glucose levels, repairing pancreatic tissue damage, and kidneys in a streptozotocin-induced rat model.
Methods: This study used a quantitative approach with an experimental design on 30 male white rats (Rattus norvegicus) divided into 6 treatment groups. STIFA Pelita Mas Herbal Oil is made by combining simplicia (Shallots, Garlic, Ginger, Curcuma zanthorrhiza, Lemongrass red, and Piper ornatum leaves) with various oils (VCO, eucalyptus oil, citronella oil, olive oil, and cinnamomum cullilawan). Diabetes was induced using streptozotocin (40 mg/kg BW) intraperitoneally. The parameters measured included blood glucose levels and histopathological changes in the kidneys and pancreas with Hematoxylin-Eosin staining. Data were analyzed using One Way ANOVA followed by the LSD or Kruskal-Wallis test.
Result: The results showed that all three herbal oil formulas were able to lower blood glucose levels, with formula 1 and formula 3 showing comparable effectiveness to glibenclamide on day 28. In histopathological observations of the kidneys, formula 3 showed the best effectiveness in repairing damage to renal tubule and glomerular cells with a damage score of 0, equivalent to normal controls. Similarly, in histopathological observations of the pancreas, formula 3 showed the highest effectiveness in repairing damage to pancreatic beta cells with a damage score of 0.2, not significantly different from normal and positive controls.
Conclusion: Stifa Pelita Mas herbal oil, especially formula 3, has the potential as an effective antidiabetic agent in lowering blood glucose levels and repairing tissue damage in the kidneys and pancreas due to diabetes. Future research should focus on dose variations to see at what dose this oil is effective.

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INTRODUCTION

Diabetes mellitus represents a significant global health problem with increasing prevalence in Indonesia. According to recent data, Indonesia ranks 5th among 10 countries with the highest diabetes prevalence, reaching 8.7% with approximately 19.5 million affected individuals, projected to increase further by 2045 (1). Data from the Central Sulawesi Provincial Health Office indicates that Bangkep district has the highest number of diabetes mellitus patients receiving standardized healthcare (4,578 people), while Touna district reports the lowest (342) (2). This epidemiological trend necessitates the development of effective and comprehensive treatment strategies, including novel therapeutic agents capable of controlling blood glucose levels with minimal side effects.

Pathophysiologically, diabetes mellitus encompasses a group of metabolic disorders characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The classification primarily includes two types: type 1 diabetes mellitus, resulting from autoimmune destruction of pancreatic β cells leading to absolute insulin deficiency, and type 2 diabetes mellitus, characterized by insulin resistance coupled with relative insulin deficiency (3). Damage to pancreatic islet β cells impairs insulin production, compromising the body's ability to regulate blood glucose levels and resulting in chronic hyperglycemia that potentially triggers various microvascular and macrovascular complications.

One of the most serious microvascular complications is diabetic nephropathy, the leading cause of end-stage renal disease (ESRD) in both developed and developing countries. Epidemiological data from the United States National Institute of Health (2007) revealed that approximately 30% of individuals with type 1 diabetes and 10% of patients with type 2 diabetes progress to diabetic kidney disease. The pathogenesis of diabetic nephropathy is multifactorial and complex, involving interrelated metabolic, hemodynamic, and inflammatory pathways. The clinical progression typically begins with asymptomatic microalbuminuria, advances to marked proteinuria, and ultimately leads to progressive decline in glomerular filtration rate, culminating in end-stage renal failure requiring renal replacement therapy.

Conventional pharmacological management of diabetes mellitus, while effective for glycemic control, frequently presents with adverse effects that diminish patients' quality of life. Oral hypoglycemic agents such as sulfonylureas can induce severe hypoglycemia, weight gain, and allergic reactions, while biguanides like metformin often cause gastrointestinal disturbances including nausea, vomiting, and diarrhea. Additionally, the financial burden of long-term treatment remains prohibitive for many patients, particularly in developing countries such as Indonesia, creating a significant barrier to effective diabetes management (4).

This therapeutic limitation has stimulated growing interest in traditional herbal medicine as a promising alternative. Natural product-based interventions for diabetes mellitus generally offer advantages of minimal side effects, affordability, and wider accessibility. This aligns with the global trend toward more holistic and sustainable healthcare approaches, where traditional medicine is increasingly integrated into modern health systems as complementary therapy.

Various preclinical and clinical studies have confirmed the therapeutic potential of natural ingredients in managing diabetes mellitus and its complications through diverse mechanisms. Virgin coconut oil (VCO) administration (5ml/kg BW for 21 days) in paraquat-induced rats has demonstrated significant improvement in kidney histoarchitecture. VCO's mechanism likely involves medium-chain fatty acids that enhance insulin sensitivity and provide antioxidant effects. Similarly, olive oil has shown capacity to repair oxidative kidney injury by increasing glutathione (GSH) levels and glutathione S-transferase (GST) activity while decreasing malondialdehyde (MDA) levels, a marker of lipid peroxidation. The active components in olive oil, particularly oleocanthal and hydroxytyrosone, are recognized for their anti-inflammatory and antioxidant properties (5–7).

Beyond vegetable oils, various medicinal plants demonstrate promising antidiabetic potential. Garlic (Allium sativum) extract exhibits hypoglycemic effects through enhanced insulin secretion, improved insulin sensitivity, and inhibition of hepatic gluconeogenesis. Organosulfur compounds in garlic, including allicin and S-allyl cysteine, contribute significantly to its antidiabetic and renoprotective activities. Phytopharmacological studies have also shown that ethyl acetate fractions from red ginger rhizome ethanol extract and dichloromethane ginger extract possess strong antioxidant activity and significant hypoglycemic effects, potentially protecting pancreatic β cells from oxidative damage while enhancing insulin secretion.

Despite extensive research on individual natural ingredients for diabetes management, limitations persist in developing formulations that integrate multiple bioactive components into practical, stable, and effective

preparations. Most previous studies have evaluated therapeutic effects of singular natural ingredients, whereas a polypharmacy approach combining several active components potentially offers superior synergistic effects in addressing the complex, multifactorial pathogenesis of diabetes mellitus.

Based on this concept, STIFA Pelita Mas Palu, a pharmaceutical higher education institution in Central Sulawesi, has developed an innovative formulation called "STIFA Pelita Mas Herbal Oil." This formulation combines various medicinal natural ingredients recognized in traditional Indonesian medicine, including garlic (*Allium sativum*), shallots (*Allium cepa*), ginger (*Zingiber officinale*), temulawak (*Curcuma xanthorrhiza*), red betel (*Piper crocatum*), lemongrass (*Cymbopogon nardus*), and several essential oils such as olive oil (*Olea europaea*), virgin coconut oil (VCO), eucalyptus oil (*Melaleuca leucadendra*), citronella oil, and star anise oil (*Cinnamomum cullilawan*).

This herbal oil formulation was developed on the principle of synergistic effects, where the combination of diverse active components is expected to mutually enhance therapeutic efficacy and simultaneously address various aspects of diabetes mellitus pathogenesis. Preliminary studies have demonstrated that this formulation exhibits good physical stability (organoleptic properties, viscosity, clarity, and pH) and moderate antioxidant activity with an IC50 value of 101.328 ppm (8). Further investigation revealed that Formula 2 STIFA Pelita Mas Herbal Oil effectively reduced urea (28.64 mg/dL) and creatinine (0.63 mg/dL) concentrations in experimental animals, indicating promising nephroprotective potential (9).

Despite these promising findings, critical research gaps remain to be addressed in developing this formulation as a phytopharmaceutical candidate for diabetes mellitus and diabetic nephropathy management. Although STIFA Pelita Mas Herbal Oil has demonstrated antioxidant and nephroprotective effects, several crucial aspects require comprehensive investigation, including histopathological alterations in kidney and pancreatic tissues and comparative efficacy assessment against established antidiabetic medications. Therefore, this study aims to evaluate: The effectiveness of STIFA Pelita Mas herbal oil in reducing blood glucose levels in streptozotocin-induced diabetic rats, the potential of the formulation in repairing pancreatic tissue damage in the diabetic model, the capacity of the formulation to ameliorate kidney histopathological alterations associated with diabetic nephropathy, and the comparative efficacy of the formulation against standard antidiabetic therapy.

Streptozotocin was selected as the diabetogenic agent due to its ability to induce selective damage to pancreatic β cells through oxidative stress and DNA fragmentation mechanisms, creating a representative experimental model of diabetes mellitus capable of developing diabetic nephropathy complications (10).

The findings of this study are expected to provide a robust scientific foundation for the development of STIFA Pelita Mas herbal oil as a phytopharmaceutical candidate for diabetes mellitus management and prevention of its complications, particularly diabetic nephropathy. Furthermore, these results may contribute to the development of alternative therapeutic strategies based on local wisdom that are effective, safe, affordable, and sustainable in addressing the global challenge of increasing diabetes mellitus prevalence and its complications.

METHOD

This study employed a quantitative approach with an experimental design. Sampling was conducted using a completely randomized design involving 30 male white rats divided into six treatment groups (one normal control, one negative control, one positive control, and three experimental formula groups). Data were analyzed using SPSS statistics version 23.

Materials and Equipment

The study utilized standard laboratory equipment for animal experimentation, pharmaceutical preparation, histopathological analysis, and biochemical testing. Key specialized equipment included a Brookfield viscometer, Olympus CX 21 light microscope (Leica), microtome, and spectrophotometer. Essential materials comprised herbal ingredients (shallots, garlic, ginger, Curcuma zanthorrhiza, red lemongrass, and Piper ornatum leaves), various oils (VCO, eucalyptus oil, citronella oil, olive oil, and Cinnamomum cullilawan), streptozotocin, glibenclamide, reagents for histopathological staining, and standard animal feed.

Ethical Approval

This study was approved by the Medical and Health Research Ethics Committee of the Faculty of Medicine, Tadulako University (Approval Number: 7110/UN 28.1.30/KL/2020). All participants, including parents or guardians for participants under the age of 18, provided informed consent before participating in the study. The confidentiality of all participants was strictly maintained throughout the research process.

Preparation of Test Animals

This study used 30 male white rats (Rattus norvegicus) divided into 6 groups. The rats were adapted for 14 days at room temperature of 20-25°C with adequate ventilation, and lighting of 12 hours dark and 12 hours light. The rats were given standard feed and drinking water ad libitum and on schedule.

Making Dry Simple Drugs

The materials in the form of Shallots, Garlic, Ginger, Curcuma zanthorrhiza, Lemongrass red, and Piper ornatum leaves are collected and then wet sorted to remove impurities such as grass, soil, and damaged plant parts. The materials are then washed with running water and shredded to a certain size, then dried for approximately 3 days. Furthermore, dry sorting is carried out to remove any remaining impurities.

Making VCO (Virgin Coconut Oil)

The making of VCO begins by separating the coconut flesh from the shell, then the coconut flesh is washed and grated. The grated coconut is added with water in a ratio of 1:1 (1 coconut is added to 1 liter of water). Coconut milk is taken by squeezing the mixture of grated coconut and water, then filtered using a cloth to separate the coconut milk and pulp. The coconut milk is then deposited in a transparent plastic container for 12 hours. After 12 hours, 4 layers will form, and the second layer from the top is taken as VCO.

Procedure for Making STIFA Pelita Mas Herbal Oil

Weighing the herbs: Shallots, Garlic, Ginger, Curcuma zanthorrhiza, Lemongrass red, and Piper ornatum leaves. Measuring olive oil (Olea europaea), virgin coconut oil (VCO), eucalyptus oil (Melaleuca leucadendra), citronella oil, and star anise oil (Cinnamomum cullilawan). Put a stainless steel pan on the stove then put VCO into the pan then heat at a temperature of 60-750C. Put in the herbs Shallots, Garlic, Ginger, Curcuma zanthorrhiza, Lemongrass red, and Piper ornatum leaves. After 15 minutes the VCO is heated then stirred until the herbs change color to blackish brown then turn off the stove. Put in eucalyptus oil, lemongrass oil, olive oil and star anise skin oil then stir until homogeneous then filtered (15).

Making Na CMC 0.5%

Na CMC as much as 0.5 grams is sprinkled in a mortar containing 10 ml of heated aquades, then stirred until evenly mixed. The Na CMC solution is put into a 100 ml measuring flask and the volume is added with aquades up to 100 ml.

Preparation of Glibenclamide Suspension 0.45 mg/kg BW

The dosage of Glibenclamide in adult humans is 5 mg/day, which if converted to rat weighing 200 grams is 0.018, then the dosage of glibenclamide for rat is 0.45 mg/kg BW. Glibenclamide tablet powder is weighed equivalent to 3.6 mg then suspended in 0.5% CMC Na up to 100 ml and stirred until homogeneous.

Preparation of Streptozotocin Induction Solution

Streptozotocin as much as 0.32 grams dissolved using citrate buffer solution with pH 4.5 to 100 ml. The dose of streptozotocin was 40 mg/kg BW, given by intraperitoneal (ip) injection.

Antidiabetic Effect Testing

A total of 30 male white rat were divided into 6 groups, adapted for 14 days in the STIFA Pelita Mas Palu animal laboratory, and given standard feed. On day 0 after adaptation, the rat were fasted for 12 hours, then initial

blood glucose levels were measured. Rat were induced intraperitoneally with streptozotocin, except for the normal control group. Blood glucose levels were measured after induction and during the treatment period.

Determination of Blood Glucose Levels

A blood sample is collected from the rat's tail tip after cleaning it with 70% alcohol and gently massaging the area. A small needle is used to prick the tail tip, and the resulting blood droplet is applied to a glucometer strip to determine blood glucose levels.

Preparation of Histopathology Preparations

The preparation of HE histopathology slides and staining of test animals involves a series of complex steps. The process begins with anesthesia of the animal to remove consciousness, followed by surgery to remove the kidney organ which is then cleaned with 0.9% NaCl. The organ sample is then fixed using 10% formalin for 48 hours to maintain the tissue structure. The next step includes dehydration to dry the tissue, clarification with xylol, and processing and embedding in liquid paraffin. After that, blocking is carried out to create a block of slides that will be sliced using a microtome with a thickness of about 5 μm. The Hematoxylin Eosin (HE) staining process involves a series of steps including deparaffinization, rehydration, staining with hematoxylin and eosin, re-dehydration, and finally mounting with entellan. The prepared slide is then observed under a microscope with a magnification of 400x to evaluate changes in kidney morphology. This entire process allows the preparation of histopathology slides that can be analyzed in depth for research or diagnostic purposes.

Data analysis

Data normality and homogeneity were assessed using Shapiro-Wilk and Levene's tests, respectively. Parametric analysis was conducted using One-way ANOVA at a 95% confidence level for normally distributed data with homogeneous variance. When these assumptions were not met, non-parametric analysis using the Kruskal-Wallis test was performed. For significant ANOVA results, post-hoc analysis with the Least Significant Difference (LSD) test was applied to identify specific differences between treatment groups. Histopathological scoring data were analyzed using the Kruskal-Wallis test followed by Mann-Whitney pairwise comparisons.

RESULTS

STIFA Pelita Mas Herbal Oil Formula

Herbal oil preparations were made with 3 formulas, namely formula 1, formula 2 and formula 3 as seen in table 1. Herbal oil preparations that have undergone physical and chemical quality evaluation and antioxidant activity tests in previous studies. Evaluation of the physical and chemical quality of herbal oils includes organoleptic tests, homogeneity tests, pH tests and viscosity tests. Testing was carried out for 21 days of storage with testing on days 1, 7, 14, and 21. The results of the antioxidant activity test of the oil and quarsetin formulas obtained IC50 values of 101.328 ppm and 4.623 ppm where the pelita mas herbal oil formula is classified as a moderate antioxidant and quarsetin is classified as a strong antioxidant. The results of the statistical analysis test, namely the normality test and the homogeneity test, stated that the data were normally distributed and homogeneous (8,11).

Table 1. STIFA Pelita Mas herbal oil formula

Material	Formula		
	F1	F2	F3
Melaleuca leucadendra	10 ml	10 ml	10 ml
Citronella oil	10 ml	10 ml	10 ml
Olea europaea	10 ml	10 ml	10 ml
Cinnamomum cullilawan	10 ml	10 ml	10 ml
Ginger	2,5 g	10 g	20 g
Curcuma zanthorrhiza	2,5 g	10 g	20 g
Garlic	2,0 g	8 g	16 g

Material	Formula		
	F1	F2	F3
Shallots	2,0 g	8 g	16 g
Lemongrass red	2,5 g	10g	20 g
Piper ornatum leaves	3 g	12 g	24 g
VCO	60 ml	60 ml	60 ml

Source: Primary Data

Based on testing and examination of the integrated testing laboratory of Gadjah Mada University, the secondary metabolite content in STIFA Pelita Mas Herbal oil was obtained, namely Alkaloids, Flavonoids, saponins, tannins and steroids in the three STIFA Pelta Mas Herbal oil preparations as seen in table 2.

Table 2. Test results for alkaloid, flavonoid, saponin, tannin and steroid levels

No.	Test Parameters	Formula			Results	Method
		Formula 1	Formula 2	Formula 3		
1.	Total Alkaloids Quinine Equivalents	0.21	1.12	2.12	%b/v	UV-vis spectrophotometry
2.	Total Flavonoid	689.62	562.79	495.82	µg/ml	UV-vis spectrophotometry
3.	Total Saponin from Quillaja Bark	0.84	1.07	1.12	%b/v	UV-vis spectrophotometry
4.	Total Tannin Acid Equivalents	495.75	211.25	377.75	mg/L	UV-vis spectrophotometry
5.	Beta Sitosterol Equivalent Steroids	1.13	1.15	1.00	%b/v	TLC

Source: Primary Data

Glucose Level Measurement Results

The results of blood glucose measurements during the treatment period (days 0, 7, 14, 21, and 28) are presented in Table 3 and Figure 1. Initial blood glucose levels (day 0) showed no significant differences between groups ($p = 0.980$), confirming homogenous baseline conditions. Following streptozotocin induction, significant differences emerged on days 7, 14, 21, and 28 (all $p < 0.001$), necessitating post-hoc analysis using the Least Significant Difference (LSD) test.

Table 3. Mean and standard deviation of blood glucose level measurement results

Day	Mean ± SD Blood Glucose Level (mg/dl)						
To-	Normal control	Negative control	Positive control	Formula 1	Formula 2	Formula 3	P
0	73± 6.70	75.4±6.70	74.4±12.73	74.2± 8.10	72±5.38	76.2±13.25	0.980
7	74.6±1.14	364± 84.8	345.8±109.69	383.4±102.93	412.2±65.92	322.2±89.05	0,000
14	75.4±1.81	311.4± 33.48	117.4± 47.40	96.2±24.89	141.2±79.01	148.2±50.65	0,000
21	74.8±0.83	289± 26.75	94.2±7.04	106.8±28.15	105±7.9	142.6±25.9	0,000
28	76.8±5.63	275.8±26.18	100.8±22.03	120±19.64	170.4±113.41	132.2±26.12	0,000

Note: Value $\rho < 0.05$ = Significantly different and Value $\rho > 0.05$ = Not significantly different

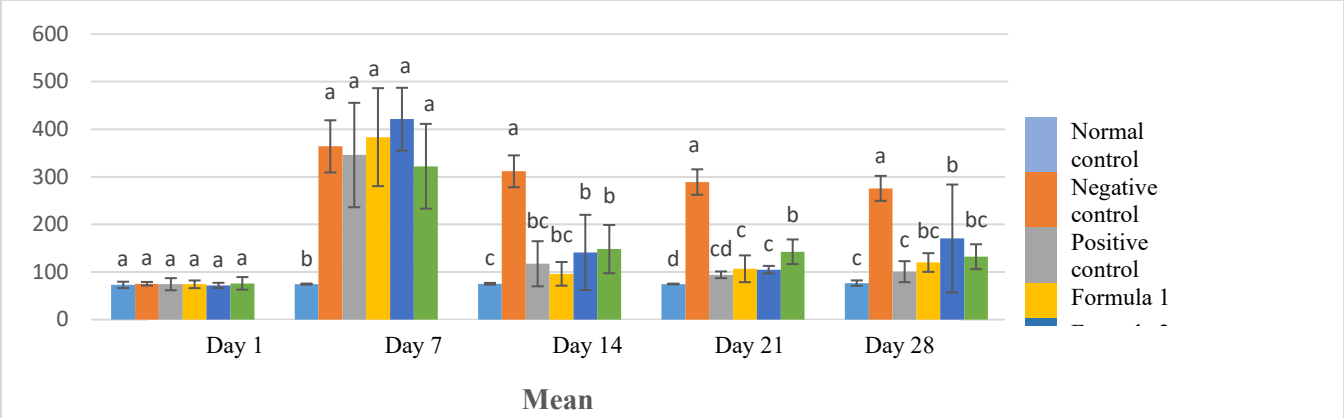

Figure 1. Blood Glucose Level Profile of Male White Rats During 28-Day Treatment Period. Data points represent mean values with different superscript letters (a, b, c, d) indicating significant differences between treatment groups at each timepoint ($p < 0.05$). Normal control maintained stable glucose levels throughout the study period. All treatment groups showed significant reduction in elevated glucose levels after streptozotocin induction, with Formula 1 and Formula 3 demonstrating efficacy comparable to the positive control (glibenclamide) by day 28.

Histopathological Observation Results

Based on the results of histopathological observations of the kidneys of male white rats (figure 2) magnification 400x with H&E staining in formulas 1 and 2, there appears to be a larger change in size and shows degenerative changes in the tubules and glomeruli (score 1 mild damage), formula 3 glomerular cells appear normal, the henle loop appears clearer showing no damage (score 0). Histopathological observations of the pancreas of male white rats (figure 3) in formula 1 show moderate damage, Langerhans cells (L) undergo apoptosis and exocrine cells (E) apoptosis and pyknosis (score 2 moderate damage), formula 2 shows mild damage, Langerhans cells (L) and exocrine cells (E) experience degenerative changes (score 1 mild damage), formula 3 looks normal, there are no changes in Langerhans cells (L) or exocrine cells (E).

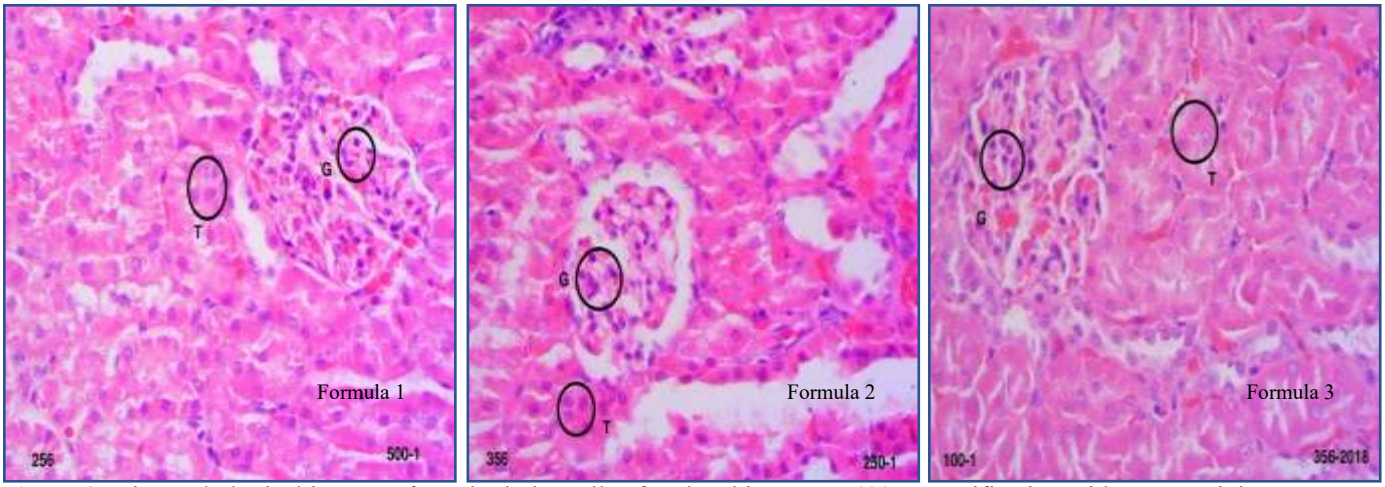

Figure 2. Histopathological images of renal tubular cells of male white rats at 400x magnification with H&E staining. Images show representative kidney sections from treatment groups: Formula 1 (mild tubular and glomerular degeneration), Formula 2 (mild tubular changes with some degeneration), and Formula 3 (normal appearance of glomeruli and tubules comparable to normal control).

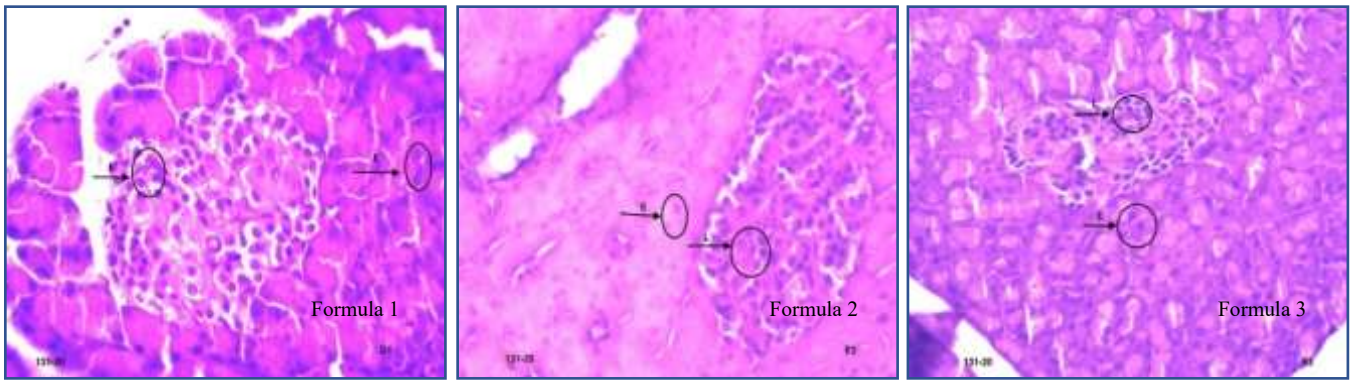

Figure 3. Histopathological images of pancreatic beta cells of male white rats at 400x magnification with H&E staining. Images show representative pancreatic sections from treatment groups: Formula 1 (moderate cellular damage with apoptotic changes), Formula 2 (mild degenerative changes), and Formula 3 (near-normal appearance of both endocrine and exocrine components comparable to normal control).

The quantitative scoring of tissue damage for kidney and pancreatic samples across all treatment groups is presented in Tables 4 and 5. Statistical analysis of these scores used a standardized damage scoring system as follows:

Score 0: No inflammatory/normal cells (0% damage)
Score 1: Normal/degenerative mild damage (≤25% damage)
Score 2: Degenerative/apoptotic/pyknotic moderate damage (25%-50% damage)
Score 3: Severe damage lysis/atrophy/apoptosis (>50% damage).

Tabel 4. Kidney Damage Level Scoring

Treatment Group	Kidney Damage Score Test Animals					Mean ± SD
	1	2	3	4	5	
Normal Control	0	0	0	0	0	0 ± 0^{a}
Negative Control	2	2	2	2	2	2 ± 0^{b}
Positive control	0	0	1	0	0	$0,2 \pm 0,44^{ca}$
Formula 1	1	1	1	1	1	1 ± 0^{d}
Formula 2	0	1	0	1	1	$0,6 \pm 0,547^{cd}$
Formula 3	0	0	0	0	0	0 ± 0^{ca}

Tabel 5. Scoring of Pancreatic Damage Level

Treatment group	Pancreatic Damage Score Test Animals					Mean ± SD
	1	2	3	4	5	
Normal Control	0	0	0	0	0	0 ± 0^{a}
Negative Control	2	2	2	2	3	$2,2 \pm 0,44^{b}$
Positive control	0	0	1	0	0	$0,2 \pm 0,44^{ca}$
Formula 1	2	1	1	1	1	$1,2 \pm 0,44^{d}$
Formula 2	0	1	1	1	0	$0,6 \pm 0,54^{cd}$
Formula 3	0	0	0	0	1	$0,2 \pm 0,44^{ca}$

Information: Different superscript letters indicate significant differences between treatments ($p < 0.05$).

DISCUSSION

Blood glucose levels of test animals (Table 3 and Figure 1) on day 0, showed normal blood glucose levels and did not differ significantly between each group. Blood glucose levels on day 7 showed a significant difference where there was an increase in blood glucose levels in all groups except normal controls. This occurred after the test animals were induced by streptozotocin. Streptozotocin works by forming reactive free radicals and can cause damage to cell membranes, proteins, and DNA, so that insulin production by β Langerhans cells is disrupted (12). Day 14

marked an important turning point in the therapeutic trajectory, with significant differences emerging across treatment groups. The antidiabetic potential of STIFA Pelita Mas herbal oil became clear because formulas 1, 2, and 3 showed glucose-lowering effects comparable to glibenclamide. In particular, formula 1 achieved normoglycemic levels that were statistically indistinguishable from normal controls, indicating a rapid and potent therapeutic action.

The differential efficacy among formulas likely reflects their varying phytochemical profiles. Formula 3, containing the highest concentration of bioactive compounds (alkaloids: 2.12%, saponins: 1.12%), demonstrated consistent glucose regulation through multiple potential mechanisms: enhanced insulin sensitivity, pancreatic β-cell regeneration, and reduced oxidative stress. This synergistic phytochemical action represents a significant advantage over conventional monotherapeutic approaches to diabetes management.

The results of histopathological examination of the kidneys with hematoxylin eoxin staining in formula 1, formula 2 and formula 3 showed a significant difference with the negative control (<0.05) which stated that the damage in the three variations of the formula had a lower level of damage compared to the negative control. Based on the scoring data, the level of kidney damage was obtained, the average level of damage was obtained, namely in the normal control having a score with an average of zero (0). This is because in the normal control, streptozotocin induction was not given so that both the tubules and glomeruli still looked normal. The negative control had an average damage score of two (2). This is because in the negative control, the test animals were given streptozotocin induction but were not given drugs, either chemical drugs or natural drugs. In the negative control, a moderate level of damage was seen where the tubule cells experienced cell degeneration while the glomerular cells experienced apoptosis. In formula 1, the average score of the level of damage is 1, this shows that there is improvement in the tubules and glomeruli after the test animals were given streptozotocin induction and received therapy from the Stifa Pelita mas herbal oil formula. In the formula 1 group, it is included in mild damage where the tubule cells are normal while the glomerular cells experience degenerative cells. In formula 2, the average score of damage is 0.6 where the tubule cells experience mild damage while the glomerular cells are still undergoing apoptosis. In formula 3, the average score of the level of damage is zero (0), this shows that there is a change in the tubule cells and glomerular cells to normal conditions after the test animals were given streptozotocin induction and received therapy from the Stifa Pelita mas herbal oil formula. In the Mann-Whitney test, the doses of formula 1 and formula 2 were significantly different from the normal control, indicating that formula 1 and formula 2 had not reached normal conditions. However, the formula 3 dose did not differ significantly from the normal control, which indicates that the formula 3 dose is an effective dose in repairing renal tubular and glomerular cells.

Based on the assessment of pancreatic beta cell damage across the six treatment groups, the normal control group exhibited an average damage score of zero (0), reflecting the absence of any treatment and consequently no damage to pancreatic beta cells. The negative control group showed an average damage score of 2.2, resulting from streptozotocin induction, which is known to cause pancreatic beta-cell damage. The positive control group demonstrated an average damage score of 0.2, as this group received therapeutic intervention with glibenclamide. Formula 1 had an average damage score of 1.2, this can be seen in Figure 3 (formula 1) where moderate damage occurred where the islets of Langerhans and exocrine cells were degenerative. Formula 2 and formula 3 had an average damage score of 0.6 and 0.2. This can be seen in Figure 3 (formula 2 and 3) where the exocrine cells and islets of Langerhans did not change or there were no inflammatory / normal cells. This shows that formula 2 and formula 3 have an effect on pancreatic cell damage.

The Mann-Whitney analysis revealed significant differences in pancreatic cell histopathology scores among the treatment groups. Specifically, the formula 1 treatment group demonstrated a moderate level of damage, with an average score of 1.2. This damage level was higher than that observed in both the normal and positive control groups, yet lower than the damage seen in the negative control group. The administration of formula 2 had a mild level of damage with an average of 0.6 where the damage value was not significantly different from the positive control, but the damage was higher compared to the normal control and lower than the negative control. The administration of formula 3 had a level of damage with an average of 0.2 where this showed no significant difference with the damage value in normal and positive controls and had a very low damage value compared to the negative control which indicated that the dose of formula 3 was an effective dose in repairing pancreatic cell damage.

The decrease in blood glucose levels and repair of kidney and pancreas damage in male white rat are caused by the content of secondary metabolites in the Stifa Pelita Mas herbal oil formula, namely flavonoids, alkaloids, saponins, tannins and steroids. Where each of these contents has an important role in reducing blood glucose levels

and regenerating kidney and pancreas cells. When viewed from the composition of the Stifa Pelita Mas herbal oil formula, the ingredient that plays a role in accelerating the absorption of substances is VCO (Virgin Coconat Oil). Where VCO contains Medium Chain Fatty Acid (MCFA) or medium chain fatty acids that are easily absorbed into cells and then into mitochondria, thereby increasing metabolism. With increased metabolism, cells will work more efficiently in forming new cells and replacing damaged cells quickly. In any condition, VCO is easily absorbed. After entering the body, VCO containing lauric acid and capric acid has a potential effect in stimulating insulin secretion by pancreatic Langerhans cells (13,14).

Flavonoids are compounds that act as antioxidants and function as the body's defense against free radicals that stop the production of ROS (Reactive Oxygen Species) so that oxidative stress does not occur which can cause kidney damage (15,16). Alkaloids can inhibit glucose absorption in the intestines so that they can reduce blood glucose levels. Alkaloids also have antioxidant activity by donating H atoms to free radicals (17). Saponins can be effective as inhibitors of the enzyme α-glucosidase, thereby reducing blood glucose levels, saponins also have antioxidant activity through free radical reduction and metal binding activity. Tannins can increase glucose and fat metabolism, thereby preventing the accumulation of both sources of calories, tannins also have antioxidant activity that can inhibit free radical chain reactions, in large amounts can be astringent (18,19).

From the results that have been obtained, when compared with the results of research conducted by previous researchers on diabetes, overall it can be said that the Stifa Pelita Mas herbal oil formula has the potential to reduce blood glucose levels. For example, when compared with the reported research on the administration of catfish oil extract as an alternative antidiabetic, it turns out that the results show that catfish oil extract has an effect on reducing blood glucose levels in white rat, with the most influential dose being a dose of 72.8 mg/kg BW with an average decrease of 87.25 mg/dl (20). When compared with the results of the research conducted, an average decrease of 120 mg/dl (F1), 170.4 (F2) and 132.2 mg/dl (F3) was obtained. This means that this study is better with a difference of 32.75 mg/dl, 83.15 mg/dl, 35.95 mg/dl, respectively. This is because catfish oil has unsaturated fats (Omega-3 and Omega-6) which are better at binding blood sugar levels and counteracting free radicals compared to Stifa Pelita Mas herbal oil.

Compared with other results in studies on black cumin oil, the average decrease was 134.5 mg/dl (21). While the results of the research conducted have decreased by 120 mg/dl (F1), 170.4 mg/dl (F2) and 132.2 mg/dl (F3) (see table 3). When compared, the research on Stifa Pelita Mas herbal oil for formula 1 and formula 3 is better with a difference of 14.5 mg/dl and 2.3 mg/dl while when compared with formula 3, the research is better with a difference of 35.9 mg/dl. This is because stifa pelita mas herbal oil has a more complex compound content considering that there are several plants that are efficacious as antidiabetics combined in the Stifa Pelita Mas herbal oil formula.

From the results of previous research conducted by researchers on pancreatic histopathology, overall it can be said that Stifa Pelita Mas herbal oil has the potential to regenerate pancreatic beta cells. When compared to the reported research on the administration of African leaf extract to regenerate pancreatic beta cells, it turns out that African leaf extract has an effect on the histopathology of the pancreas of male white rat with an effective dose of 150 mg/kgBW with an average damage of 0.8 (22). When compared with the results of the research that has been done, the results of the damage scoring in formula 1 are 1.2, formula 2 is 0.6 and formula 3 is 0.2, so the research on herbal oil formulas for formula 2 and formula 3 is better with a difference of 0.2 and 0.6 respectively, while with formula 1 is better than previous research with a difference of 0.4. This is because stifa pelita mas herbal oil has a higher alkaloid content than African leaf ethanol extract which functions to regenerate damaged pancreatic beta cells. The results of previous research on ketapang bark extract reported that a dose of 120 mg/kgBW was effective in regenerating pancreatic beta cells with a damage score level of 1.25 (23). While the results of the research conducted obtained an average damage scoring result of 1.2 (formula 1), 0.6 (formula 2), and 0.2 (formula 3) (see table 5). When compared, the research on herbal oil stifa pelita mas that has been done is better than previous research with differences of 0.05, 0.65 and 1.05 respectively. This is because the content of compounds in herbal oil stifa pelita mas which play a role in regenerating damaged pancreatic beta cells has a greater amount compared to ketapang bark extract.

In a study of water apple leaves on the histopathological picture of the pancreas of male white rat, it was shown that water apple leaf extract was able to regenerate pancreatic beta cells at an effective dose of 300 mg/KgBW with an average damage of 1.33 (24). Meanwhile, when compared with the research that has been done (see table 5), the research on stifa pelita mas herbal oil is better with an average difference of 0.13, 0.73, and 1.13 respectively.

This is because stifa pelita mas herbal oil has a better secondary metabolite compound content compared to water apple leaf extract in regenerating damaged pancreatic beta cells. The results of the study of ethanol extract of Pandan Wangi Leaves (*Pandanus Amaryllifolius Roxb*.) at a dose of 600 mg/kg BW have an effect on regenerating kidney tissue in male white rat with a damage level of 0.6 (25), equivalent to formula 2 with a damage level of 0.6, but when compared to formula 3 which is much better with a damage score of 0.

Overall, the results of this study indicate that the STIFA Pelita Mas herbal oil formula has promising potential as an antidiabetic agent with the ability to lower blood glucose levels and regenerate damage to the kidneys and pancreas. Formula 3 showed the highest effectiveness in regenerating kidney cells and pancreatic beta cells with very low levels of damage (score 0 for kidney and 0.2 for pancreas), equivalent to normal controls and positive controls. The content of secondary metabolites such as flavonoids, alkaloids, saponins, tannins, and steroids play an important role in this therapeutic effect, with a synergistic effect from the combination of herbal ingredients. The composition of VCO in the formula also contributes to increased absorption of active substances due to the content of medium-chain fatty acids that are easily absorbed into cells and increase metabolism. Compared with similar studies using catfish oil extract, black cumin oil, African leaf extract, ketapang bark extract, and water apple leaf extract, the STIFA Pelita Mas herbal oil formula showed better results in lowering blood glucose levels and regenerating tissue damage, especially in formula 2 and formula 3.

CONCLUSION

This study investigated the potential of STIFA Pelita Mas herbal oil formulas as antidiabetic agents and evaluated their effectiveness in lowering blood glucose levels and repairing histopathological damage of kidney and pancreas in streptozotocin-induced rats. The findings showed that all three herbal oil formulas were able to significantly lower blood glucose levels, with formula 1 and formula 3 showing equivalent effects to glibenclamide on day 28, highlighting the potential of herbal-based therapies in the management of diabetes.

In particular, formula 3 showed the highest regeneration ability in kidney cells (damage score 0) and pancreatic beta cells (damage score 0.2), which were not significantly different from normal controls. These results underline the important role of secondary metabolites such as flavonoids, alkaloids, saponins, tannins, and steroids in antidiabetic activity and tissue regeneration, suggesting that these herbal oil formulations may be a promising alternative in the management of diabetes and its related complications.

Although this study provides valuable insights into the effectiveness of herbal oils in diabetes management, some limitations need to be noted, such as the lack of determination of the optimal dosage of STIFA Pelita Mas herbal oil. Future studies should focus on dose-response relationships to identify the minimum effective dose, evaluate long-term effects and safety profiles, and further elucidate the specific mechanisms by which these formulations exert their antidiabetic and tissue-regenerative effects. These additional investigations would strengthen the evidence base for potential clinical applications of STIFA Pelita Mas herbal oil in diabetes management.

AUTHOR'S CONTRIBUTION STATEMENT

Each author contributed equally to this work. Investigation (Joni Tandi, Tien Wahyu Handayani, Muthmaina Tuldjanah), supervision (Joni Tandi), administration (Tien Wahyu Handayani), writing and editing (Muthmaina Tuldjanah). All authors approved the submission of the manuscript to this journal and gave final approval for publication. In addition, they agree to be fully accountable for all aspects of this work.

CONFLICTS OF INTEREST

We as authors declare that we have no conflict of interest whatsoever.

DECLARATION OF GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

The authors declare that they did not use Generative AI or AI-Assisted Technologies during the writing of this manuscript.

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