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ANTIDIABETIC POTENTIAL OF SOLID LIPID NANOPARTICLES (SLNS) FROM KABAU SEED (*ARCHIDENDRON BUBALINUM* (JACK) I.C. NIELSEN) EXTRACT COATED WITH TRIMYRISTIN

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ABSTRACT

[***Antidiabetic Potential of Solid Lipid Nanoparticles (Slns) from Kabau Seed (Archidendron Bubalinum (Jack) I.C. Nielsen) Extract Coated With Trimyristin***]Type 2 diabetes mellitus is a global health problem that continues to increase. One alternative approach in managing diabetes is using natural materials with antihyperglycemic activity. This study aims to evaluate the effectiveness of solid lipid nanoparticles (SLN) containing Kabau seed extract (*Archidendron bubalinum* (Jack) I.C. Nielsen) coated with trimyristin in reducing blood glucose levels in hyperglycemic rats. Extraction was carried out by maceration using 96% ethanol, while SLN was synthesized by high-speed homogenization and ultrasonication methods. Particle size analysis showed an average diameter of 262.61 nm with a polydispersity index (PDI) of 0.144, indicating a homogeneous formulation. Phytochemical testing showed that Kabau seed extract contains alkaloids, flavonoids, tannins, and saponins contributing to antihyperglycemic activity. In vivo tests on *Mus musculus* showed that 20 % concentration of Kabau SLN reduced blood glucose levels by up to 97 mg/dL, approaching the effectiveness of metformin (104 mg/dL). Statistical analysis of ANOVA and BNT test showed significant differences between treatments. These results indicate that Kabau SLN has the potential as a candidate for phytopharmaceuticals in managing type 2 diabetes mellitus.

Keywords: *Diabetes mellitus; Kabau; solid lipid nanoparticles; trimyristin; flavonoids*

INTRODUCTION

Diabetes mellitus, particularly type 2 diabetes, has become a global health crisis, with a significant burden in Asia and the Pacific. The prevalence of type 2 diabetes is projected to increase substantially by 2044, especially in low and middle socio-demographic index (SDI) regions [1][2]. Indonesia ranks among the top 10 countries with the highest

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diabetes prevalence at 10,8%, with an estimated 10 million cases [3][4]. The global prevalence of type 2 diabetes is projected to increase to 7079 per 100,000 individuals by 2030, with lower-income countries showing concerning rising trends [5]. In Indonesia, a study of hospitalized type 2 diabetes patients revealed a 6.6% in-hospital mortality rate, with factors such as advanced age, comorbidities, and severe complications contributing to increased mortality risk [6]. Ketoacidosis emerged as the most significant risk factor for in-hospital mortality. The rising prevalence of diabetes poses substantial social, economic, and healthcare challenges, necessitating urgent preventive measures and improved management strategies to address this growing public health concern [2][5].

Diabetes mellitus (DM) is characterized by hyperglycemia due to impaired insulin secretion, action, or both [7]. Type 2 diabetes mellitus (T2DM) accounts for 90% of all diabetes cases and is caused by insulin resistance in target cells [7][8]. Risk factors for T2DM include family history, obesity, smoking, hypertension, coronary heart disease, lack of rest, and stress [7]. A case-control study by Harefa and Lingga [9] found significant associations between T2DM and overweight, physical inactivity, hypertension, age, and family history. T2DM pathophysiology involves defective insulin secretion by pancreatic β-cells and impaired insulin response in insulin-sensitive tissues. The disease is associated with accelerated atherosclerosis development and increased cardiovascular risk. Prevention and management of T2DM should focus on modifiable risk factors and understanding the molecular mechanisms involved in insulin metabolism [8].

Recent studies have explored traditional and herbal treatments for diabetes as alternatives to conventional therapies. Indonesia, with its rich biodiversity, has numerous plants traditionally used for diabetes management [10]. One such plant is *Archidendron bubalinum* (Jack) I.C. Nielsen (Kabau), which has shown potential antidiabetic activity in animal studies. Ethanol extracts of Kabau leaves demonstrated a 33% reduction in blood glucose levels in hyperglycemic rats at a dose of 1000 mg/kg BW [11]. Ethanol extracts of Kabau leaves demonstrated significant blood glucose reduction in alloxan-induced diabetic rats, with the most effective dose being 1000 mg/kg BW [12]. Similarly, Kabau seed powder suspension at 1000 mg/kg BW showed promising antidiabetic activity in alloxan-induced diabetic rats [13]. Further research on Kabau seed extracts revealed that the ethanol extract and methanol fraction exhibited the most potent antidiabetic effects, comparable to glibenclamide, using various screening methods [12]. The antidiabetic properties of Kabau are attributed to its phytochemical constituents, including flavonoids, phenolics, and saponins, which may contribute to improved glucose metabolism and antioxidant effects. These herbal remedies are believed to be effective due to their bioactive compounds and natural antioxidants, offering potential benefits with fewer side effects compared to conventional treatments [14].

Recent advancements in drug delivery technology have led to the development of lipid-based nanocarriers, particularly solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs), which offer improved drug stability and delivery [15]. These nanocarriers, typically ranging from 1 to 1000 nm in diameter, consist of a solid

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lipid core stabilized by surfactants [16]. They provide numerous advantages, including biodegradability, non-toxicity, high drug loading capacity, and enhanced bioavailability of various bioactive compounds [17]. Surface modification of these nanocarriers using polymers, ligands, surfactants, and fatty acids can further improve their targeting ability, drug penetration, and controlled release properties [18]. Their unique properties make them a promising alternative to conventional drug delivery systems and polymeric nanoparticles [15].

Despite promising findings on the antidiabetic properties of Kabau seed (*Archidendron bubalinum*) extract, there remains a significant research gap in its formulation using solid lipid nanoparticles (SLNs), particularly those coated with trimyristin, a material known for enhancing drug delivery efficiency. Trimyristin, a triglyceride predominantly found in nutmeg seeds, has been identified as a key lipid constituent [19]. The ethyl acetate fraction of nutmeg seed extract, which includes trimyristin, has demonstrated anti-butyrylcholinesterase activity, suggesting its potential bioactivity that may contribute to glucose-lowering effects when used as a coating agent.

Existing studies have largely focused on crude extracts, lacking a detailed investigation into nanocarrier-based delivery systems that could improve bioavailability and therapeutic effect. Additionally, pharmacokinetic and pharmacodynamic data are scarce to support clinical application. Addressing this gap is urgent due to the rising global prevalence of diabetes and the pressing need for safer, more effective, and natural treatment alternatives that leverage advancements in nanotechnology. Based on the background described above, this study aims to explore the potential of solid lipid nanoparticles (SLNs) formulated from Kabau seed extract (*Archidendron bubalinum* (Jack) I.C. Nielsen) and coated with trimyristin in effectively reducing blood glucose levels.

RESEARCH METHODS

Extraction of Kabau Seeds (*Archidendron bubalinum* (Jack) I.C. Nielsen)

A total of 600 g of Kabau seed extract (*Archidendron bubalinum (Jack) I.C. Nielsen*) was extracted by maceration using 2.5 L of 96% technical ethanol solvent in a glass jar. Then the sample was placed in a clean room that was not exposed to direct light for 3 days with occasional stirring.

The maceration results were separated using filter paper. The filtrate obtained was then concentrated using a rotary evaporator to obtain a crude extract. The crude extract obtained will be used to manufacture solid lipid nanoparticles of trimyristin from Kabau seed extract (*Archidendron bubalinum* (Jack) I.C. Nielsen) using high-speed homogenization and ultrasonication methods.

Isolation of Trimyristin from Nutmeg

Nutmeg powder simplicia (60 g) was wrapped in a Soxhlet bag and put into a Soxhlet apparatus. 250 mL of n-hexane solvent was added to a round-bottom flask, then heated in a water bath. Ethanol was added to the resulting extract, then heated in a water bath at 60 °C for 15 minutes. The solution was then poured into an Erlenmeyer flask and cooled. Crystallization will be slow, leaving the mixture at room temperature for approximately 1 hour. Then, cool the mixture in ice water for 30 minutes.

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Synthesis of SLNs Kabau seeds (*Archidendron bubalinum* (Jack) I.C. Nielsen)

The synthesis of solid lipid nanoparticles using high-speed homogenization and ultrasonic techniques was carried out at a temperature of 55 ºC. This experiment was carried out in the following steps

a. The lipid phase, consisting of 5 g of trimyristin and 0.5 g of Kabau seed extract (*Archidendron bubalinum* (Jack) I.C. Nielsen), was heated at a temperature of 55 ºC while stirring.
b. The aqueous phase, consisting of 5 g of Tween 80, 5 g of maltodextrin and 34.5 mL of distilled water, was heated at 55 ºC until dissolved. c. Both phases were homogenized at a speed of 20,000 rpm for 15 minutes to form a homogeneous SLNs dispersion.
c. The SLNs dispersion was then ultrasonicated for 30 minutes then dried using a freezer dryer at a temperature of up to -40ºC. The SLNs powder is stored in a closed container protected from light at room temperature.

Particle Size Analyze

A total of 10 mL of Kabau seed solid lipid nanoparticle colloid was measured using PSA (Particle Size Analyzer) Beckman Coulter in IPB physics laboratory. This measurement aims to determine the average particle size, size distribution, and homogeneity (polydispersity index) of the SLNs formulation.

Particle size analysis (PSA) is crucial for characterizing nanoparticle samples and evaluating their homogeneity. Laser diffraction PSA can assess sample homogeneity by measuring particle size distributions. The polydispersity index (PDI) is a key parameter for evaluating size consistency, with lower values indicating higher uniformity

Screening of Secondary Metabolites

The phytochemical screening was carried out based on the method of [20] to identify secondary metabolites such as alkaloids, flavonoids, saponins, terpenoids, steroids, and tannins.

Blood Glucose Testing Procedure

a. SLNs Solutions

The extract and solid lipid nanoparticles (SLNs) of Kabau seeds (*Archidendron bubalinum* (Jack) I.C. Nielsen) were prepared at a concentration of 33%. To obtain this concentration, 3 mL of Kabau seed extract was measured and placed into a beaker, followed by adding 8 mL of distilled water using a volumetric pipette. Similarly, the SLN solution was prepared by taking 3 mL of the SLN formulation of Kabau seed extract and adding 8 mL of distilled water to achieve a 33% concentration.

b. 1% Na-CMC Solution

One gram of Na-CMC was weighed and placed into a mortar, then ground with 1 mL of hot water. The mixture was left to stand for a few minutes, then ground again until a homogeneous gel was formed. After that, distilled water was added gradually using a 100 mL volumetric pipette. The mixture was transferred into a 100 mL volumetric flask, and the volume was adjusted to the mark with distilled water.

c. 20% Glucose Solution

Twenty grams of glucose were placed into an Erlenmeyer flask. Then, 50 mL of distilled water was added using a volumetric pipette. The mixture was stirred until the glucose was completely dissolved. Afterward, the solution volume was adjusted to 100 mL with additional distilled water.

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d. Metformin Suspension

One tablet of metformin (500 mg/kg body weight) was used as a positive control. If the dose conversion value from humans to mice weighing 200 g is 0.0252 [28][40], then the dose of metformin for mice is 0.0252 mg/200 g BW or for rats weighing 30 g, then:

$$30\ \text{g BW} \times \frac{1\ g}{200\ g} \times 0{,}0252 \frac{\text{mg}}{200\text{g}} \text{BW} = 0{,}00378\ \text{g metformin}$$

Metformin 500 mg was placed into a mortar and ground into a fine powder. Then, 50 mL of 1% Na-CMC (sodium carboxymethyl cellulose) solution was gradually added while grinding until a homogeneous suspension was obtained. The suspension was then transferred into a 100 mL volumetric flask, and the volume was adjusted to 100 mL with an additional 1% Na-CMC solution.

e. Animal Testing

The test animals used were mice (Mus musculus), aged 2–3 months, with body weights ranging from 20 to 30 grams. A total of 40 mice were used and randomly divided into seven treatment groups. Before treatment, the test animals were fasted for 16 hours. Baseline blood glucose levels were then measured. Following this, all animals were grouped and intravenously induced with EDTA at a dose of 150 mg/kg body weight. Subsequently, they were administered 20% glucose solution and continued to receive standard feed.

After three days, blood glucose levels were re-measured to confirm that EDTA induction effectively maintained a hyperglycemic state. The mice were then divided into seven treatment groups, each consisting of 3 mice:

Table 1. Treatments Group of Mices

GROUP	TREATMENT
P1 (Negative Control)	Feed + EDTA + 20% glucose + 1% Na-CMC
P2 (Positive Control)	Feed + EDTA + 20% glucose + metformin + 1% Na-CMC
P3	Feed + EDTA + 20% glucose + 20% Kabau seed extract + 1% Na-CMC
P4	Feed + EDTA + 20% glucose + SLN of 5% Kabau seed extract + 1% Na-CMC
P5	Feed + EDTA + 20% glucose + SLN of 10% Kabau seed extract + 1% Na-CMC
P6	Feed + EDTA + 20% glucose + SLN of 15% Kabau seed extract + 1% Na-CMC
P7	Feed + EDTA + 20% glucose + SLN of 20% Kabau seed extract + 1% Na-CMC

After treatment, the mice were returned to their respective cages and given food and water ad libitum. Blood glucose levels were measured on days 1, 4, and 7 as the final evaluation points.

f. Determination of Blood Glucose Levels

Before use, the glucometer is turned on, and a glucose test strip is inserted. According to Pradha et al [21], blood glucose measurement is performed by collecting a blood sample from the tail vein of the mouse. The blood drop is placed onto the glucometer strip, which is then read by the device. Within approximately 10 seconds, the blood glucose level is displayed on the glucometer screen. Blood glucose levels were recorded at several stages: baseline (before induction), post-induction, and after treatment. The data were analyzed to evaluate changes in blood glucose levels across the seven treatment groups. The results were statistically analyzed using a Completely Randomized

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Design (CRD) and One-Way ANOVA at a 95% confidence level to determine if there were significant differences between the treatments. If a significant difference was found, the test analysis was continued with the Least Significant Difference (LSD) or BNT to identify which treatment groups differed significantly. The percentage reduction in blood glucose levels and the treatment effectiveness were calculated using the following formulas:

$$Effectiveness\ (\%) = \frac{\%Protection\ of\ Kabau\ Seed\ Extract\ or\ Nanoparticle\ Group}{\%\ Protection\ of\ positive\ control\ group} x\ 100\%$$

RESULTS AND DISCUSSION

Plant Determination

Plant determination is an activity that recognizes a plant's identity or character. The results of the determination show that the plant used is indeed a kabab seed (*Archidendron bubalinum (Jack) I.C. Nielsen (Jack) I.C. Nielsen*), with the following taxonomic levels.

Kingdom : Plantae
Division : Spermatophyta
Class : Dicotyledoneae
Order : Fabales
Family : Fabaceae
Genus : Archidendron
Species : Archidendron bubalinum (Jack) I.C. Nielsen (Jack) I.C. Nielsen

Secondary Metabolite Compounds of Kabau Seed Extract (Archidendron bubalinum (Jack) I.C. Nielsen)

The results of the test of secondary metabolite compounds contained in Kabau Seed Extract can be seen in Table 2.

Table 2. Phytochemical Screening Results of Kabau Seed Extract (*Archidendron bubalinum* (Jack) I.C. Nielsen)

Secondary metabolites	Results	
Alkaloids	No precipitate (Dragendorff)	-
	Brown precipitate (Wagner)	+
	White precipitate (Mayer)	+
Flavonoids	Brown	+
Terpenoids	Orange-red	-
Tanins	Dark green	+
Saponins	Stable foam	+

Based on Table 2, it is known that the results of the phytochemical test of the ethanol extract of Kabau seeds have been proven to contain alkaloid, flavonoid, tannin and saponin compounds which have a mechanism as a natural blood glucose-lowering drug.

Flavonoids, naturally occurring plant compounds, show promising potential in managing type 2 diabetes mellitus (T2DM) and its complications. These compounds exhibit antidiabetic properties by improving glucose tolerance, enhancing pancreatic β-cell function, and increasing insulin secretion [22]. Flavonoids like kaempferol can activate mitochondrial calcium uptake in β-cells, potentiating glucose-induced insulin secretion [23]. They also modulate the insulin signaling pathway, though the exact mechanism and optimal dosage remain unclear [24]. Flavonoids demonstrate multiple beneficial effects, including antioxidant and anti-inflammatory actions, regulation of glucose and lipid metabolism, and management of insulin resistance [25]. Quercetin, a specific flavonoid, has shown

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potential in improving oral glucose tolerance and inhibiting enzymes that affect glucose metabolism [22]. These findings suggest that flavonoids could be valuable in developing novel treatments for T2DM and its associated complications.

Alkaloids from medicinal plants show significant potential as antidiabetic agents through various mechanisms. They can inhibit key enzymes like α-glucosidase and α-amylase, reducing glucose absorption in the digestive system [26][27]. Alkaloids also enhance insulin secretion and sensitivity, increase glucose uptake, and exhibit antioxidant properties [26]. They can inhibit advanced glycation end products (AGEs) formation and improve cellular glucose metabolism [29]. Additionally, alkaloids protect pancreatic beta cells, repair abnormal insulin signaling, and activate AMP-activated protein kinase (AMPK) [30]. These compounds offer advantages over synthetic drugs due to their safety profile and ability to maintain internal homeostasis [29]. The diverse mechanisms of action make alkaloids promising candidates for diabetes management, either as monotherapies or in combination with existing treatments [29][30].

Saponins are glycosides bound to steroids or triterpenes, known for their diverse biological activities including anticancer and hypoglycemic effects [31][32]. These compounds can induce apoptosis, inhibit cellular invasion, and possess antioxidant properties [31]. In diabetes management, saponins and related compounds like β-sitosterol have shown promise in reducing blood glucose levels and improving insulin sensitivity [33][34]. β-sitosterol, a plant-derived compound, has been found to alleviate inflammation and insulin resistance in adipose tissue by downregulating inflammatory pathways such as IKKβ/NF-κB and JNK [34]. Additionally, it restores serum levels of pro-inflammatory cytokines and increases anti-inflammatory adipocytokines in diabetic rats [34]. These findings suggest that saponins and related compounds may offer potential therapeutic benefits for diabetes and cancer treatment.

Tannins and other plant secondary metabolites have shown potential in managing diabetes and lowering blood glucose levels. Tannins can improve meat and milk quality in animals, while exhibiting antioxidant, antibacterial, antiviral, and anti-inflammatory properties [35]. Catechins, a type of tannin, can alleviate hyperglycemia by improving insulin resistance, reducing oxidative stress, and regulating intestinal function [36]. Various plant-derived compounds, including tannins, target carbohydrate metabolism pathways, protect pancreatic beta cells, and inhibit carbohydrate digestion and absorption [30]. A study on Clinacanthus nutans extract, which contains antioxidants, demonstrated its ability to significantly lower blood glucose levels in diabetic Wistar rats, with the most effective dose being 75 mg/kg body weight [33]. These findings highlight the potential of tannins and other plant-derived compounds in diabetes management and blood glucose regulation.

Particle Size Analysis

Nanoparticle size plays a critical role in determining stability, bioavailability, and overall effectiveness in drug delivery systems[37]. In this study, Particle Size Analyzer (PSA) was used to characterize the size and uniformity of the solid lipid nanoparticles (SLNs) derived from Kabau seed extract. The analysis was carried out using the Cordouan Technology Nano-Q, an advanced instrument capable of measuring particle sizes within the 1–1,000 nm range[38].

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Beyond measuring the average particle diameter, PSA also provides insight into the homogeneity of particle distribution through the Polydispersity Index (PDI). The PDI is a key parameter to evaluate the consistency of nanoparticle sizes in a sample. According to [39], a PDI value between 0.01 and 0.7 indicates a narrow size distribution (monodisperse), suggesting high uniformity. Conversely, a PDI value above 0.7 reflects a broader size distribution, indicating a less homogeneous formulation.

From the PSA results, the nanoparticles exhibited an average size of 262.61 nm and a PDI value of 0.144. This low PDI suggests that the nanoparticle formulation is highly uniform and monodisperse, reflecting a good level of homogeneity[39]. Moreover, such a value is indicative of a stable nanoparticle system, which is essential for maintaining consistent performance during application. These results are visually supported by the analysis image presented below.

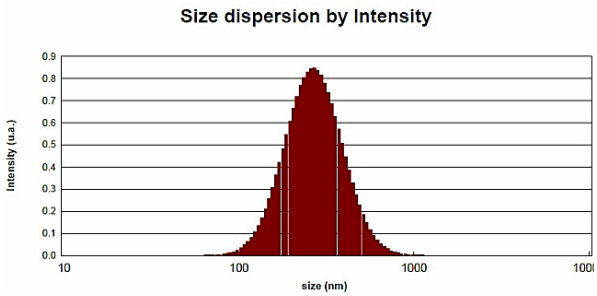

Figure 1. Particle size distribution

Effect of Concentration of Kabau Seed Extract (Archidendron bubalinum (Jack) I.C Nielsen) on Decreasing Blood Glucose Levels

Before being given Kabau seed extract (*Archidendron bubalinum* (Jack) IC Nielsen), mice were exposed to hyperglycemic conditions conditioned by administering EDTA 150 mg/Kg BB. Mice were fasted for 16 hours before being given treatment. The aim is to limit dietary factors that can affect blood glucose levels in mice. After fasting, the blood glucose levels of mice were estimated using a glucometer.

After checking the basic blood sugar levels, the mice were rested for 30 minutes, then the mice were induced using EDTA (Ethylene Diamine Tetraacetic Acid). The regulatory ability of EDTA is to create hyperglycemic conditions that last for several days. EDTA can damage fundamental substances in pancreatic β cells, causing reduced insulin in pancreatic β cells

The blood glucose levels of mice obtained after being induced with EDTA were 179-191 mg/dL. This is in accordance with the requirement that for the occurrence of hyperglycemia in test animals is when the blood glucose levels of the test animals reach ≥120 mg/dL

The next treatment is the administration of Kabau seed extract (*Archidendron bubalinum (Jack) I.C Nielsen*) and solid lipid nanoparticles of Kabau seed extract (*Archidendron bubalinum (Jack) I.C Nielsen*) to mice, after which the extract and nanoparticles are given rest and given food and drink as usual. Checking the blood glucose levels of mice is carried out on days 1, 4 and 7.

The average decrease in blood glucose levels can be seen in Table 3.

Table 3. Average Initial Blood Sugar Levels

Treatment	Initial Blood Glucose (mg//dL)	Blood Glucose After Induction (mg/dL)	Blood Glucose After Treatment	Blood Glucose Decrease (mg/dL)
Negative Control	82	180	162	18
Positive Control	85	190	86	104
Extract 20%	83	192	130	62
SLN Extract 5%	76	182	128	54
SLN Extract 10%	80	182	120	62
SLN Extract 15%	84	183	90	93
SLN Extract 20%	86	184	87	97

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The results in Table 3 show that the average normal blood glucose of mice ranges from 76.00 to 86.00 mg/dL, after EDTA induction, it ranges from 182-192 mg/dL. To find out how much blood glucose decreases in mice, the difference between blood glucose levels after induction and blood glucose levels after administration of extract and solid lipid nanoparticles of Kabau seeds (*Archidendron bubalinum (Jack) I.C Nielsen*) is calculated. The results of the decrease in blood glucose levels can be done by calculating the blood glucose levels after EDTA induction minus the blood glucose levels after treatment. Then the average is calculated as shown in Table 3. The average decrease in blood glucose levels was greatest in the positive control, namely 104 mg/dL, then the 20% Sln concentration was 97 mg/dL. The graph showing the decrease in blood glucose in mice is shown in Figure 2.

Figure 2. Measurement of blood glucose levels in mice in various treatments

Figure 2 shows that the average blood glucose levels showed significant differences between the various treatments. The differences were seen from groups P1 to P7, namely P1 as a negative control, P2 as a positive control (metformin), P3 was given 20% kabau leaf extract, P4 to P7 were Sln with various concentrations of extract, P4 Sln kabau seed extract 5%, P5 Sln kabau seed extract 10%, P6 Sln kabau seed extract 15%, and P7 Sln kabau seed extract 20%.

The positive control group showed a drastic decrease in blood glucose levels due to the mechanism of action of metformin, namely lowering blood glucose levels by directly stimulating glycolysis in peripheral tissues, increasing glucose absorption from the blood, decreasing gluconeogenesis in the liver, slowing glucose absorption from the intestines, decreasing plasma glucagon levels, and increasing insulin binding to peripheral insulin receptors. Metformin functions primarily by increasing glucose transport into muscle cells and increasing insulin sensitivity by increasing insulin binding in peripheral tissues.

The significant differences between the seven treatments were determined by statistical analysis using one-way ANOVA based on a completely randomized design (CRD). The results of the ANOVA test between the seven treatments have a significance value of 97.65 > 3.12. This means there is a significant effect between the 7 treatments of extract and solid lipid nanoparticles of Kabau seeds on reducing blood glucose in mice. This indicates that the seven groups have quite different effectiveness in reducing blood glucose levels.

Futhermore, the smallest significant difference test (LSD) or BNT was conducted to determine the differences in each treatment group. The results of the statistical analysis of the BNT test can be seen in Table 4.

Table 4. Average Results of the BNT Test

Treatment	Average Blood Glucose Decrease (mg/dL)	Average + BNT	Notation
Negative Control	18	19,95164	A
Sln extract 5%	54	55,95164	B
extract 20%	62	63,95164	C
SLN extract 10%	62	63,95164	C
SLN extract 15%	93	94,95164	D
SLN extract 20%	97	98,95164	E
Positive Control	104	105,9516	F

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The results of the LSD (Least Significant Difference) or BNT test presented in Table 4 indicate that there are similarities in the antidiabetic effects among certain treatment groups. The lowest and highest statistical notations were assigned to the negative control and positive control (metformin) groups, respectively, highlighting the contrast between untreated and standard drug-treated animals. A notable similarity was observed between the group treated with 20% Kabau leaf extract and the group treated with 10% concentration of solid lipid nanoparticle (SLN) extract, suggesting that at these concentrations, both formulations produce comparable glucose-lowering effects.

However, treatments with SLN extract concentrations of 15% and 20% exhibited significantly different effects compared to other groups. This indicates a dose-dependent increase in the effectiveness of SLN formulations, where higher concentrations resulted in a more pronounced reduction in blood glucose levels. These differences further support the hypothesis that formulation type (conventional extract vs. SLN) and concentration play crucial roles in the bioavailability and therapeutic efficacy of the extract. SLN formulations likely enhance cellular uptake and stability of the active compounds, contributing to their greater antidiabetic activity at higher concentrations.

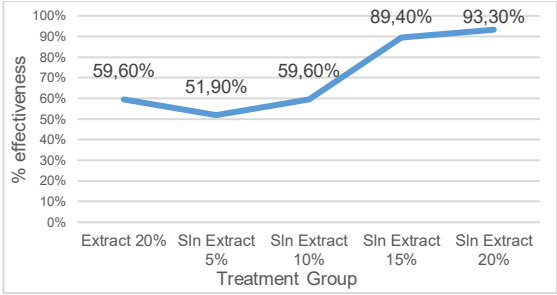

Figure 3. Percentage of Effectiveness of Test Materials

Figure 3 illustrates the comparative effectiveness of varying concentrations of the kabau seed extract and its SLNs formulation (*Archidendron bubalinum (Jack) I.C Nielsen*) in reducing blood glucose levels. Notably, as shown in Figure 3, the SLNs formulation at 20% concentration demonstrated the highest glucose reduction efficacy with a percentage of 93.30%, closely followed by the 15% concentration at 89.40%. Conversely, the lowest effectiveness was observed at the 5% concentration, with a value of 51.90%. Interestingly, the 10% concentration of the SLNs showed comparable effectiveness to the 20% concentration of the crude kabau seed extract, suggesting an enhanced bioavailability or improved delivery mechanism through the nanoparticle system.

Statistical analysis using anova confirmed a significant positive correlation between the concentration of SLNs and the percentage of glucose reduction, indicating that increasing the concentration of the kabau seed extract SLNs leads to greater hypoglycemic effects. These findings highlight the potential of SLNs as an efficient delivery system that can enhance the therapeutic efficacy of kabau seed extract in managing blood glucose levels.

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CONCLUSION

This study demonstrates that solid lipid nanoparticles (SLNs) formulated with *Archidendron bubalinum* (Kabau) seed extract and coated with trimyristin exhibit significant antihyperglycemic activity in hyperglycemic mice. The SLNs showed favorable particle size characteristics (average 262.61 nm, PDI 0.144), indicating a stable and homogeneous formulation. Phytochemical screening confirmed the presence of active compounds such as flavonoids, alkaloids, tannins, and saponins, which are known for their antidiabetic properties. In vivo testing revealed that the 20% concentration of SLN formulation effectively reduced blood glucose levels, with performance approaching metformin. Statistical analysis confirmed significant differences among treatments, supporting the efficacy of SLN formulations over crude extracts. These findings suggest that Kabau seed SLNs hold promise as a natural and efficient alternative for type 2 diabetes management, with potential for further development in pharmaceutical applications.

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