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Antidiabetic and Antihyperuricemic Activities of Salak Madu (Salacca edulis Reinw) Peel Extract in Alloxan- and High-Purine Diet-Induced Mice

Dzulrifaad Ubaidillah Al Afza[1]*, Neli Syahida Ni'ma[1]

[1]Department of Pharmacy, Faculty of Medicine, Universitas Negeri Semarang, Semarang, 50229, Indonesia

*Correspondence to: *dzulrifaad@students.unnes.ac.id*

Abstract: Diabetes mellitus (DM) is a chronic metabolic disorder characterized by impaired carbohydrate, lipid, and protein metabolism. Hyperuricemia is a condition in which serum uric-acid levels exceed normal values, namely > 7.0 mg/dL in men and > 6.0 mg/dL in women. Both antidiabetic and antihyperuricemic therapies can be administered pharmacologically and non-pharmacologically; however, synthetic drugs often produce undesirable side effects. Concerns regarding these adverse effects have led many people to favour herbal remedies that are perceived as safer, one of which is the Salak Madu fruit. Salak Madu (Salacca edulis Reinw.), an emerging premium variety cultivated in Sleman, Yogyakarta, is rich in flavonoids with potential antihyperglycemic and antihyperuricemic properties. The present study evaluated the antidiabetic and antihyperuricemic activities of Salak Madu peel extract in vivo using alloxan-induced and high-purine-diet mouse models. Mice were observed over 14 days and treated orally with peel extract at doses of 100, 200, and 400 mg/kg body weight (BW). On day 14, the 100 and 200 mg/kg BW doses produced significant reductions in blood-glucose levels ($P < 0.05$), indicating a marked antihyperglycemic effect in hyperglycemic mice. For serum uric-acid reduction, significant effects were observed on day 7 at doses of 200 and 400 mg/kg BW ($P < 0.05$), demonstrating a pronounced antihyperuricemic action in hyperuricemic mice.

Keywords: Salak Madu, antidiabetic, antihyperuricemic, in vivo

INTRODUCTION

Diabetes mellitus (DM) and hyperuricemia are two metabolic disorders that are increasingly prevalent worldwide. The coexistence of these conditions presents a higher risk for cardiovascular complications and metabolic syndrome. DM is characterized by chronic hyperglycemia caused by either insulin deficiency or resistance, leading to impaired metabolism of carbohydrates, fats, and proteins. It is one of the major health concerns worldwide, with over 537 million adults affected globally according to the International Diabetes Federation (IDF) 2021 report. In Indonesia alone, the prevalence of DM has shown a continuous increase, contributing significantly to national healthcare burdens. Hyperuricemia, defined as elevated serum uric acid levels beyond normal thresholds, is often associated with DM and may worsen insulin resistance. Several studies have indicated that increased uric acid levels could impair pancreatic β-cell function and exacerbate oxidative stress, thereby contributing to the pathophysiology of DM. Conversely, hyperinsulinemia seen in early-stage type 2 diabetes can impair uric acid excretion through the kidneys, establishing a bidirectional relationship between the two conditions.

While conventional treatments such as metformin for DM and allopurinol for hyperuricemia are commonly used, their associated adverse effects, including gastrointestinal discomfort and allergic reactions, necessitate the exploration of safer alternatives. In recent years, interest has grown in the use of herbal medicines due to their perceived safety, cost-effectiveness, and multi-target therapeutic mechanisms. Salak Madu (Salacca edulis Reinw), a tropical fruit endemic to Indonesia, is traditionally consumed for its health-promoting properties. Preliminary studies suggest that the peel of this fruit contains various bioactive compounds, including flavonoids, known for their antioxidant, antidiabetic, and antihyperuricemic activities. Despite the promising pharmacological profile of Salak Madu peel, scientific investigations validating its efficacy in in vivo models remain limited. Therefore, this study was conducted to evaluate the dual activity of Salak Madu peel extract in reducing blood glucose and serum uric acid levels in mice induced with alloxan and a high-purine diet. By exploring the antidiabetic and antihyperuricemic effects of this natural extract, we aim to provide a scientific basis for its potential use as a functional herbal therapy for managing metabolic disorders.

METHODS

Experimental Design

This study employed a randomized experimental method with a pretest-posttest control group design. Twenty-five

male Swiss Webster mice aged 8 weeks and weighing 20–30 g were acclimatized for one week under standard laboratory conditions (22 ± 2°C, 12-hour light/dark cycle) with ad libitum access to food and water. Mice were then randomly divided into five groups (n=5):

- Negative Control Group: induced with alloxan and high-purine diet but received no treatment
- Positive Control Group: induced with alloxan and high-purine diet, treated with metformin (65 mg/kg BW) and allopurinol (10 mg/kg BW)
- Treatment Group I: induced with alloxan and high-purine diet, treated with Salak Madu peel extract 100 mg/kg BW
- Treatment Group II: induced with alloxan and high-purine diet, treated with Salak Madu peel extract 200 mg/kg BW
- Treatment Group II: induced with alloxan and high-purine diet, treated with Salak Madu peel extract 400 mg/kg BW

Treatments were administered orally once daily for 14 days.

Extraction Process

Fresh Salak Madu fruits were collected from Srumbung, Magelang. The peels were separated, cleaned, and air-dried at room temperature without direct sunlight. The dried material was powdered and macerated in 96% ethanol in a 1:5 (w/v) ratio for five days. The macerate was filtered and concentrated using a rotary evaporator to obtain a thick extract.

Induction of Diabetes and Hyperuricemia

Diabetes mellitus was induced using a single intraperitoneal injection of alloxan monohydrate (150 mg/kg BW) dissolved in 0.9% NaCl. After 72 hours, fasting blood glucose levels were measured. Hyperuricemia was induced by oral administration of a high-purine diet consisting of chicken liver juice (1 mL) daily for 7 days.

Phytochemical Screening

In this study, qualitative phytochemical screening was performed to identify the secondary metabolite compounds present in the Salacca zalacca var. amadensis (honey salak) peel extract. The screening included tests for flavonoids, alkaloids, saponins, tannins, and terpenoids. The phytochemical screening was conducted by observing color changes upon the addition of specific reagents (Sahputra, 2008).

Measurement of Blood Glucose and Uric Acid

Blood samples were collected from the tail vein. Glucose and uric acid levels were measured using a digital Glucose-Cholesterol-Uric acid (GCU) meter on days 0 (baseline), 7, and 14. Data were analyzed using one-way ANOVA followed by Tukey's post hoc test. A p-value < 0.05 was considered statistically significant.

RESULT AND DISCUSSION

Moisture Content Loss

The moisture content loss test aims to determine the amount of water and volatile compounds present in the extract. A moisture content exceeding 10% may lead to enzymatic activity and microbial degradation (Manoi, 2006). Based on calculations, the moisture content loss was found to be 0.021%, which meets the acceptable standard of less than 10% as stated in the Indonesian Herbal Pharmacopoeia, 2nd Edition (2017).

Water Content

The determination of water content aims to quantify the amount of water contained in the extract. The calculation yielded a water content of 0.011%, which complies with the standard requirement of less than 10% (Indonesian Herbal Pharmacopoeia, 2nd Edition, 2017).

Extract Yield

Yield refers to the ratio of the weight of the concentrated extract obtained to the initial weight of the simplicia used. A higher yield value indicates a greater amount of extract produced (Nahor et al., 2020). In this study, 500 grams of simplicia produced 13.70 grams of thick extract, resulting in a yield of 2.74%. Although this value is below the expected minimum standard of 10% according to the Indonesian Herbal Pharmacopoeia, 2nd Edition (2017), it still reflects an acceptable extraction efficiency considering the type of material used.

Phytochemical Screening

Table 1. Phytochemical identification results

Classes of secondary metabolites	XXX
Flavonoids	+
Alkaloids	-
Tannins	+
Saponins	-
Steroids	-
Terpenoids	-

The phytochemical screening results in table 1 showed that the ethanolic extract of Salacca zalacca var. amadensis (honey salak) peel contains classes of compounds including flavonoids and tannins. A study by Rohaeti et al. (2022) reported that the ethanolic extract of Salacca zalacca fruit peel from the Manonjaya variety contains active flavonoid compounds, specifically glycosylflavones and flavones, which were shown to reduce blood glucose levels in alloxan-induced test animals. The presence of flavonoid and tannin compounds in salak fruit was also confirmed by Sahputra (2008), who stated that the peel extract of Salacca zalacca var. pondoh contains flavonoids, tannins, and a small amount of alkaloids. Furthermore, a study by Widowati et al. (2025) analyzed the phytochemical composition of Salacca zalacca fruit extract using LC-MS/MS and identified the presence of epicatechin, naringenin, and apigenin.

Blood Glucose Levels

The antihyperglycemic activity of Salak Madu peel extract was evaluated by measuring fasting blood glucose levels in mice on days 0, 7, and 14. On day 0, all groups except the normal control had glucose levels exceeding 200 mg/dL, confirming successful induction of hyperglycemia. By day 14, the groups treated with extract at 100 mg/kg BW and 200 mg/kg BW showed statistically significant reductions in blood glucose levels compared to the negative control group ($p < 0.05$). The 400 mg/kg BW group also showed glucose reduction, although the significance was not consistent across all data points. Among the extract-treated groups, the 100 mg/kg BW dose showed the most consistent and significant reduction in glucose levels from day 0 to day 14. This suggests that this dose may be optimal for antihyperglycemic effect. These findings indicate that Salak Madu peel extract possesses antidiabetic properties, likely mediated through the bioactive flavonoid components such as quercetin, naringenin, and epicatechin, which are known to enhance insulin sensitivity, promote glucose uptake in peripheral tissues, and support β-cell function. Other phytochemicals like tannins and saponins may also contribute synergistically.

Uric Acid Levels

Serum uric acid levels were evaluated on days 0, 7, and 14. After induction with a high-purine diet, mice in the negative control group showed elevated serum uric acid levels. On day 7, groups receiving 200 mg/kg BW and 400 mg/kg BW of the extract showed a statistically significant decrease in serum uric acid levels compared to the negative control ($p < 0.05$). The extract's activity may be linked to flavonoids that inhibit xanthine oxidase—the enzyme responsible for converting hypoxanthine to uric acid. Quercetin and apigenin, found in Salak Madu peel, have been previously reported to inhibit xanthine oxidase activity and reduce oxidative stress in renal tissue, promoting enhanced uric acid clearance. One of the limitations of this study was the measurement capacity of the uric acid analyzer used. The instrument was unable to detect or measure serum uric acid levels below 3.00 mg/dL. As a result, data falling below this threshold could not be accurately recorded, potentially affecting the overall analysis of uric acid-lowering effectiveness. This limitation was particularly evident on day 14, during which several data points could not be measured, leading to incomplete and less accurate results.

Discussion

This study supports the potential dual benefit of Salak Madu peel extract in reducing both blood glucose and serum uric acid levels in vivo. The effectiveness of the extract at 200 mg/kg BW was consistently notable for both outcomes. The observed antihyperglycemic and antihyperuricemic effects may be attributed to the combined activity of several bioactive compounds, particularly flavonoids, which work through diverse mechanisms: antioxidant action, inhibition of carbohydrate-hydrolyzing enzymes, enhancement of insulin signaling, and inhibition of purine metabolism. The study demonstrates the added value of utilizing Salak Madu peel, an agricultural byproduct, as a sustainable source for the development of herbal medicine. However, this study was limited by its sample size and duration. Future research should focus on isolating the active constituents, validating their mechanisms, and conducting chronic toxicity studies to establish long-term safety and therapeutic potential.

CONCLUSION

This study demonstrates that Salak Madu (Salacca edulis Reinw) peel extract possesses significant antidiabetic and antihyperuricemic effects in vivo. Oral administration of the extract at doses of 200 mg/kg and 400 mg/kg BW resulted in notable reductions in blood glucose and serum uric acid levels in alloxan- and high-purine diet-induced mice. These effects are likely mediated by the presence of flavonoids and other bioactive compounds that act through multiple mechanisms, including enhancing insulin sensitivity, modulating glucose metabolism, and inhibiting xanthine oxidase activity. The findings suggest that Salak Madu peel extract has promising potential as a natural therapeutic agent for the integrated management of diabetes mellitus and hyperuricemia. As an accessible and underutilized plant resource, it may offer a sustainable alternative to conventional pharmacotherapy, particularly in resource-limited settings. Further research is warranted to elucidate the pharmacodynamics, optimal dosage, and clinical applicability of this herbal extract.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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