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# Evaluation of the antidiabetic activity of ethyl acetate partition of ekor naga leaves (*Rhaphidophora pinnata* (L.f) Schott) on male white mice induced by alloxan

**Fathnur Sani Kasmadi[1], Maimum[1], Yuliawati[1], Indri Maharini[1], Vinka Lupita Sari[1], Tia Wida Ekaputri Hz[2], Tengku Arief Buana Perkasa[3]**

[1] Pharmacy Study Program, Faculty of Medicine and Public Health Sciences, Universitas Jambi, Telanaipura, Telanaipura District, Jambi City, Jambi, Postal Code 36361, Indonesia
[2] Medical Study Program, Faculty of Medicine and Public Health Sciences, Universitas Jambi, Telanaipura, Telanaipura District, Jambi City, Jambi, Postal Code 36361, Indonesia
[3] Department of Biochemistry and Medical Biology, Faculty of Medicine and Health Sciences, Universitas Jambi, 36361, Jambi, Indonesia

* Coressponding Authors: fathnursanik@unja.ac.id

## Abstract

**Background:** Diabetes mellitus is a condition where blood glucose levels increase due to a decrease in the amount or sensitivity of insulin produced by the body. Previous research has shown that the ethanol extract of Ekor Naga leaves (*Rhaphidophora pinnata* (L.f.) Schott) has potential as an antidiabetic agent. The extract also contains several secondary metabolic compounds such as flavonoids and phenolics, which are suspected to have antidiabetic potential. **Objective:** This research aims to investigate the activity of ethyl acetate partitioning of Ekor Naga leaves extract (*Rhaphidophora pinnata* (L.f.) Schott) in reducing blood sugar levels in diabetic mice. **Methods:** This research employed a Completely Randomized Design (CRD) method with six treatments: a normal control, a glibenclamide positive control, a Na-CMC negative control, and treatment groups with doses of 125, 250, and 500 mg/kg body weight (BW) of the ethyl acetate partition of ekor naga leaves extract. The observed parameter was the average decrease in blood sugar levels over a 21-day period.**Results:** The results were analyzed using the one-way ANOVA test, followed by Duncan's multiple range test. The research showed that the ethyl acetate partition of Ekor Naga leaves can reduce blood sugar levels in mice over 21 days. The results have shown significant improvement in blood sugar levels between treatment groups. The best dose in reducing blood glucose levels was 500 mg/KgBW with a percentage decrease of 58.98%.**Conclusion:** Ethyl acetate partition of ekor naga leaves has potential as an antidiabetic agent.

**Keywords:** Ekor naga leaves; antidiabetic; blood sugar; partition; alloxan

## Cite This Article

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## INTRODUCTION

Diabetes is a disease caused by high blood glucose levels. High blood glucose levels result from insufficient or insensitive insulin production. There are two types of diabetes: type 1, which occurs when the beta cells of the pancreas are no longer able to produce insulin, resulting in high glucose levels and hyperglycemia; and type 2, which is characterized by insulin resistance and impaired insulin secretion. Type 2 diabetes mellitus occurs when the beta cells of the pancreas are no longer sensitive to glucose in the body. This condition is often caused by multiple factors, including obesity, lifestyle, and hereditary diseases[1], [2], [3].

The number of people living with diabetes has consistently increased, rising from 200 million in 1990 to 830 million in 2022. This rapid increase occurred in low- and middle-income countries compared to high-income countries. Diabetes worsens with the emergence of comorbidities such as cardiovascular disease and kidney disease. A healthy diet, regular physical activity, maintaining a normal body weight, and avoiding smoking are key factors in preventing or delaying the onset of diabetes[4], [5], [6].

Indonesia is a tropical country rich in various medicinal plants, so the use of traditional medicines, as a traditional heritage, remains highly sought after by the Indonesian people[7], [8], [9]. One plant with potential antidiabetic effects is Ekor Naga leaves. Previous research has shown that the ethanol extract of Ekor Naga leaves has potential as an antihyperglycemic and antidiabetic agent in alloxan-induced test animals. The results showed that the ethanol extract of Ekor Naga leaves, administered at a dose of 250 mg/kg, improved blood glucose levels over a 21-day treatment period[10].

The separation of extracts using the partition method involves separating compounds found in plants[11], [12], [13]. This separation is carried out by separating the polarities of the compounds, specifically n-hexane, ethyl acetate, and n-butanol. The ethyl acetate fraction obtained from this partition will be used for further testing of the Ekor Naga leaves extract, which has potential as an antidiabetic agent.

## METHODS

### *The simplicia preparation of ekor naga leaves*

Collected Ekor Naga leaves are wet-sorted to remove impurities and washed. The leaves are cut into small pieces and oven-dried at 40°C. Then, the leaves are ground into a fine powder using a grinder.

### *Ekor naga leaves extract*

Seven hundred fifty grams of Ekor Naga leaves powder was macerated using 70% ethanol at a ratio of 1:10. The maceration process was carried out for 2 x 24 hours, with stirring occurring 5 to 6 times per 24 hours. The maceration results were filtered and collected as a macerate. Remaceration was repeated twice with a 1 x 24-hour soaking process. All the macerate results were heated in a rotary evaporator at 50°C until a thick extract was obtained.

### *Ekor naga leaves extract partition process*

Ekor Naga leaves extract was partitioned using solvents of varying polarities by a liquid-liquid partition method, employing solvents of increasing polarity: distilled water, n-hexane, ethyl acetate, and n-butanol. The partition process was carried out by dissolving 100 grams of Ekor Naga leaves extract in 100 mL of distilled water. Then, partition with 250 mL of n-hexane solvent, which was repeated 3 times. The extract, which was soluble and insoluble in n-hexane, was separated by partitioning using 250

mL of ethyl acetate, with three repetitions. Then, finally, partition with n-butanol. All partition results were thickened using a rotary evaporator until a thick extract was obtained. The ethyl acetate partition results will be used for further testing as an antidiabetic agent.

### *Antidiabetic activity test of ekor naga leaves extract*

The test animals used in this research were healthy male white mice weighing 200-250 grams. Each treatment group consisted of five mice. The treatment groups were: Normal: Rats without treatment; Negative Control: Alloxan-induced Rats without therapy; Positive Control: Rats were induced by alloxan and received glibenclamide therapy of 0.45 mg/kg BW; Treatment 1: Alloxan-induced Rats have received Ekor Naga leaves extract therapy at a dose of 125 mg/kg BW; Treatment 2: Alloxan-induced Rats have received Ekor Naga leaves extract therapy at a dose of 250 mg/kg BW; Treatment 3: Alloxan-induced Rats have received Ekor Naga leaves extract therapy at a dose of 500 mg/kg BW.

Before alloxan induction, the blood glucose levels of the test animals were measured using a glucometer by taking blood samples from the thigh veins of Rats. The Rats were then fasted for 12 hours. After fasting, Rats were induced with alloxan at a dose of 175 mg/kg BW dissolved in 0.9% physiological NaCl and administered intraperitoneally at a volume of 0.2 mL/20 grams BW. After three days, blood sugar levels were measured; if the blood sugar level exceeded 200 mg/dL, the rats were considered diabetic. The antidiabetic effect of Ekor Naga leaves extract was measured on days 0, 7, 14, and 21 using a glucose test strip with a glucometer (Easy Touch GCU®).

### *Statistical analysis*

The research results were analyzed in two ways: descriptively (extracting characteristics) and using a one-way ANOVA test (blood sugar), with significant changes calculated at $p < 0.01$, and then followed by a further Duncan's test.

## RESULTS

Determination of the Ekor Naga leaf plant was conducted at the Jatinangor Herbarium, Padjajaran University. The results have indicated that the plant used in this research was an Ekor Naga plant with the scientific name Raphidophora pinnata (L.f.) Schott, registered with the registration number 07/HB/03. The yield of the extract obtained after maceration of 750 grams of Ekor Naga leaves powder was 16% with an ethyl acetate partition yield of 9.88%. Table 1 presents the results of observations on non-specific parameters of the ethyl acetate partition that meet the requirements, specifically that the thick extract should have a yield below 10%[14].

**Table 1.** Non-specific parameters of the ekor naga leaves extract partition results

| Parameter | Results± SD |
|---|---|
| Water Content | 7,9% ± 1,05 |
| Ash Content | 7,6% ± 0,57 |

Phytochemical screening is an initial identification method for herbal products. The phytochemical screening results from ethyl acetate partition have shown that the extract contained flavonoids, alkaloids, and tannins. These results differ from the screening results of the Ekor Naga leaves extract, as reported in research conducted by Sani et al. (2022)[15]. The difference in results was due to the use of different solvents

in the partition process, which varied in their polarity levels. So it produces different compounds depending on the level of polarity.

Diabetes induction in this research was achieved using alloxan. Alloxan is an organic compound with the formula OC(NHCO)2C(OH)2. It is a toxic glucose analog that selectively destroys insulin-producing cells in the pancreas (beta cells) and can be administered to rodents. The dose of alloxan given in this study was 175mg/kg BW. Rats will be included in the treatment group if their blood glucose level after induction is above 200 mg/dL, except for the normal group, which does not receive treatment[16], [17], [18], [19]. Before induction, blood sugar levels were in the range of 62.8-130 mg/Kg BW. After induction, blood sugar levels increased above 200 mg/dL, to 383 to 530.75 mg/dL. Improvements in blood sugar levels have been shown in Table 2, which displays the observed changes in blood sugar levels during treatment on days 0, 7, 14, and 21. Statistically, there was a significant difference compared to the negative control. The results of the ethyl acetate partition have shown that a dose of 500 mg/kg BW gave the best potential as an antidiabetic agent. These were followed by doses of 250 mg/kg BW and 125 mg/kg BW.

**Table 2**. Average blood sugar levels during 21 days of administration of ethyl acetate partition results of the Ekor Naga leaves.

| Treatement | Mean Blood Glucose (mg/dL) ± SEM | | | |
|---|---|---|---|---|
| | 0 Days | 7 Days | 14 Days | 21 Days |
| Normal | 101.5±8.59$^{a}$ | 189.00±11.92$^{a}$ | 156.00±7.45$^{a}$ | 117.75±6.70$^{a}$ |
| Positive Control(Glibenklamid) | 418.50±77.37$^{b}$ | 315.50±94.79$^{a,b}$ | 229.25±60.53$^{a,b}$ | 131.25±25.02$^{a,}$ |
| Negative Control (NaCMC 0,5%) | 530.75±15.49$^{b}$ | 330.67±85.67$^{a,b}$ | 437.50±873.45$^{c}$ | 440.50±73.88$^{c}$ |
| Dose 1 (125mg/KgBB) | 398.00±49.05$^{b}$ | 429.75±81.05$^{a,b}$ | 319.50±85.62$^{a,b,c}$ | 236.50±79.72$^{a}$ |
| Dose 2 (250mg/KgBB) | 517.25±49.97$^{b}$ | 536.75±48.59$^{b}$ | 397.25±40.40$^{b,c}$ | 223.00±27.67$^{a}$ |
| Dose 3 (500mg/KgBB) | 383.50±76.30$^{b}$ | 242.00±92.76$^{a}$ | 228.00±59.14$^{a,b}$ | 151.00±34.79$^{a}$ |

The inducer used in this research was alloxan. Alloxan increases blood sugar levels by The results have shown a significant increase in blood sugar levels after the 3rd day of induction compared to before induction. Blood sugar levels before induction ranged from 62.8 to 135 mg/dL, while after induction, they were consistently above 200 mg/dL. This condition indicates the success of the induction process[20], [21], [22]. Blood glucose data after 21 days of treatment have shown a significant decrease between treatment groups. The difference in average blood glucose levels indicates that the ethyl acetate partitioning of Ekor Naga leaves has the potential to lower blood glucose levels. The percentage reduction in blood glucose levels on day 21 was 44.77% for dose 1, 55.86% for dose 2, and 58.98% for dose 3. Meanwhile, for the positive control, it was 64.68%.

The ability of the Ekor Naga leaf ethyl acetate partition to lower blood glucose levels is supported by the presence of secondary metabolite compounds, including flavonoids, alkaloids, and tannins. Flavonoids, alkaloids, and tannins function as antioxidants, protecting beta cells from damage and enhancing insulin sensitivity. In addition, these three compounds also play a role in stimulating the alpha-glucosidase and alpha-amylase enzymes by breaking down carbohydrates and playing a role in inhibiting GLUT 2 (Glucose Transporter Type 2) phosphodiesterase, so that cAMP in beta cells will become more sensitive to secreting insulin, so that insulin production increases and blood sugar levels will decrease[23], [24], [25], [26].

## CONCLUSIONS

The ethyl acetate extract of Ekor Naga leaves (dosages of 125 mg/Kg BW, 250 mg/Kg BW, and 500 mg/Kg BW) exhibits antidiabetic activity, as indicated by a decrease in blood sugar levels in test animals over 21 days of treatment. Statistically, there was a significant difference between the treatment groups ($p < 0.05$), with the best treatment dose being 500 mg/Kg BW (58.98%).

## CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## DECLARATION OF ARTIFICIAL INTELLIGENCE USE

The authors declare that this article was not created using Artificial Intelligence (AI) tools. All scientific content, findings, and data interpretation are entirely the work and responsibility of the authors.

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