

## ANTIDIABETIC EFFECT OF ETHANOLIC EXTRACT OF KEDONGDONG PAGAR LEAVES (*Lannea coromandelica* (Houtt.) Merr.) ON MALE MICE

**Safriana<sup>1\*</sup>, Melati Yulia Kusumastuti<sup>1</sup>, Andilala<sup>2</sup>**

<sup>1</sup>Departement of Pharmacy, Sekolah Tinggi Ilmu Kesehatan Indah Medan, Jalan Saudara Ujung No. 110 Simpang Limun, Medan, 20226, Indonesia

<sup>2</sup>Departement of Diploma III Nursery, Sekolah Tinggi Ilmu Kesehatan Indah Medan, Jalan Saudara Ujung No. 110 Simpang Limun, Medan, 20226, Indonesia

\*Email Corresponding: [safrianaabdullah@gmail.com](mailto:safrianaabdullah@gmail.com)

Submitted: January 30, 2024 Revised: February 22, 2024 Accepted: March 13, 2024

### ABSTRACT

Diabetes mellitus is a metabolic condition defined as an increase in blood glucose levels (hyperglycemia) caused by impaired insulin production or insulin action. One of the treatments for diabetes mellitus is the use of medicinal plants because they contain bioactive phytochemicals. Kedondong pagar leaves (*Lannea coromandelica* (Houtt.) Merr.) is an empirical medication used to reduce the blood glucose levels in Aceh, Indonesia. The leaves contain flavonoids, which have antioxidant effects that can reduce damage to the pancreatic beta cells. The goal of this study was to examine the antidiabetic impact of an ethanol extract of kedondong pagar leaves in male mice induced with alloxan to increase blood glucose levels. The test procedure involved splitting 25 mice into five treatment groups, Na-CMC suspension 0.5% w/v, Kedondong pagar extract with dose 10 mg/kg BW, 20 mg/kg BW, 40 mg/kg BW, and glibenclamide suspension with dose 0.65 mg/kg BW as positive control. The results showed that all ethanolic extracts of *Lannea coromandelica* had the same potency to lower blood glucose levels in mice, implying that the ethanol extract of *Lannea coromandelica* leaves had antidiabetic activity due to the presence of antidiabetic compounds such as flavonoids and glycosides.

**Keywords:** Antidiabetic, Diabetic, Kedondong Pagar Leaves, *Lannea coromandelica*.

### INTRODUCTION

Diabetes mellitus is a global health concern owing to its high morbidity and death rates (Triplitt, Repas, and Alvarez 2017). Diabetes is defined by hyperglycemia (an increase in blood glucose levels), which causes a variety of short-term metabolic problems in protein and fat metabolism, as well as permanent alterations in blood glucose levels over time. Diabetes can lead to various microvascular and macrovascular problems over time (Brahmachari 2010). There are two main types of diabetes mellitus: i. Type 1 diabetes, also known as insulin-dependent diabetes mellitus (IDDM), is caused by a lack of insulin secretion by pancreas beta cells. ii. Type 2 diabetes, also known as non-insulin-dependent diabetes mellitus (NIDDM), is caused by the decreased sensitivity of target tissues to insulin (Ozougwu 2013).

Diabetes mellitus can be managed medically using drugs and injections. However, this option is not always feasible because of the high cost of medical care. Diabetes mellitus is also treated naturally using medicinal herbs. The possibility of its management by oral administration of hypoglycemic agents has stimulated great research interest over the years. Although different types of oral hypoglycemic agents are available along with insulin for the management of diabetes mellitus, there is an increased demand for the use of herbal

preparations with hypoglycemic activity (Osinubi, Ajayi, and Adesuyan 2005). Plants with therapeutic effects are readily available and can be harvested either fresh or dried. Traditional therapy with medicinal herbs provides an alternative approach to overcome this problem (Wijayakusuma 2002).

Recently, plant secondary metabolites have received considerable attention as sources of therapeutic compounds (Krishnaraju et al. 2005). Kedondong pagar leaves (*Lannea coromandelica* (Houtt.) Merr.) is said to have medical use, particularly as an antidiabetic, because heated water has been used for centuries to reduce blood glucose levels.

## RESEARCH METHOD

The study procedures used included collecting and processing plant materials, producing extracts, preparing experimental animals, and assessing the antidiabetic activity of the ethanolic extract from kedondong pagar leaves in male mice.

### 1. Materials Collection

Kedondong pagar plants were collected from Desa Samakurok, Kecamatan Tanah Jambo Aye, Kabupaten Aceh Utara, Nanggroe, Aceh Darussalam. It was identified by the Indonesian Institute of Sciences with number of 1824/IPH.1.02/If.8/2013. Mice (*Mus musculus*) were used as animal models according to ethical guidelines approved by the Health Research Ethics Committee of the Faculty of Medicine, University of Muhammadiyah Sumatera Utara (number 481/KEPK/FKUMSU/2020).

### 2. The process of making extracts

The extract was produced by maceration in an ethanol solvent. Dried sample powder (500 g) was placed in a jar and soaked in 5 L of 70% ethanol. Subsequently, the sample was allowed to stand for 18 hours by mixing for a certain period. Macerate was separated using filtering. The filtering procedure was performed twice with the same quantity and quality of the solvent, as previously described. All macerates were collected, and the macerate was concentrated using a rotary evaporator. The samples were then freeze-dried for approximately 24 hours (Depkes RI, 2008).

### 3. Test of antidiabetic activity

The antidiabetic effect of an ethanolic extract from kedondong pagar leaves was tested in alloxan-induced mice. Alloxan can cause diabetic by harming pancreatic beta cells. The ethanolic extract of kedondong pagar leaves was orally administered once daily for 7 days. The treatments were divided into five groups: negative control (CMC-Na 0.5%), positive control (glibenclamide dosage 0.65 mg/kg BW), group I (10 mg/kg BW), group II (20 mg/kg BW), and dosage group III (40 mg/kg BW). The blood sugar level (mg/dL) for each group was measured with a glucometer (Easy Touch® GCU) after 30 minutes oral distribution for 7 days. Blood samples were collected from mice's tails around 1 drop and placed in a glucometer that had already been calibrated based on the strip test (Dewinta, Mukono, and Mustika 2020).

### 4. Data Analysis

The data were analyzed using SPSS version 20. To assess homogeneity and normality, the data were examined using the Kolmogorov-Smirnov technique. One-way analysis of variance was used One Way ANOVA to obtain the mean variance between groups. If there were differences, a post-hoc Tukey HSD test was performed to identify true differences between treatments.

## RESULTS AND DISCUSSION

The kedondong pagar plant belongs to the Anacardiaceae family and has green leaves, have compound shape, odd pinnate, leaf veins pinnate, leaf width 4.4 - 5.0 cm, leaf length 7.3 - 10.5 cm, and leaf stalk length 0.3 - 0.8 cm, while simplicia kedondong pagar leaves are brownish green and have a shriveled shape (Safriana et al. 2021). These images are shown in Figure 1.



**Figure 1.** The appearance of Kedondong Pagar Leaves (a) Fresh and (b) Dry

The results of phytochemical screening showed that the simplicia and ethanol extracts of kedondong pagar leaves contain secondary metabolite compounds, namely flavonoids, glycosides, saponins, tannins, and steroids/triterpenoids, as shown in [Table I](#) ([Safriana et al. 2021](#)).

**Table I.** Phytochemical Screening Results of Simplicia Powder And Ethanol Extract of Kedondong Pagar Leaves

Screening	Simplicia	Extract
Alkaloid	-	-
Flavonoids	+	+
Glycosides	+	+
Saponins	+	+
Tannins	+	+
Steroids/triterpenoids	+	+

-: does not contain compounds; +: contain compounds

#### Antidiabetic activity

The mice were divided into five treatment groups, each with five mice: the control group received a 0.5% w/v Na-CMC the suspension of 1% bw, the experiment group received an ethanolic extract from kedondong pagar leaves the suspension that a dose of 10 mg/kg BW (body weight), 20 mg/kg BW, 40 mg/kg BW, and glibenclamide the suspension at a dose of 0.65 mg/kg BW as a positive control. Before induction with alloxan at a dosage of 125 mg/kg BW, the mice were starved for 18 hours. Fasting blood glucose levels were measured with a glucometer. Blood glucose levels were approximately 75-87 mg/dl ([Table I](#)), and the mice were administered an injection of alloxan at a dosage of 125 mg/kg BW via their abdomens. Their behavior and overall weight were examined for three days. Blood sugar levels were determined on third day before treatment ([Datu, Lebang, and Suoth 2023](#)). Mice with blood sugar levels  $\geq 139$  mg/dL were classified as having diabetes ([C. E. Wulandari, Pudjadi, and Kartikawati 2010](#)). [Table II](#) shows the blood sugar levels before and after alloxan induction in mice.

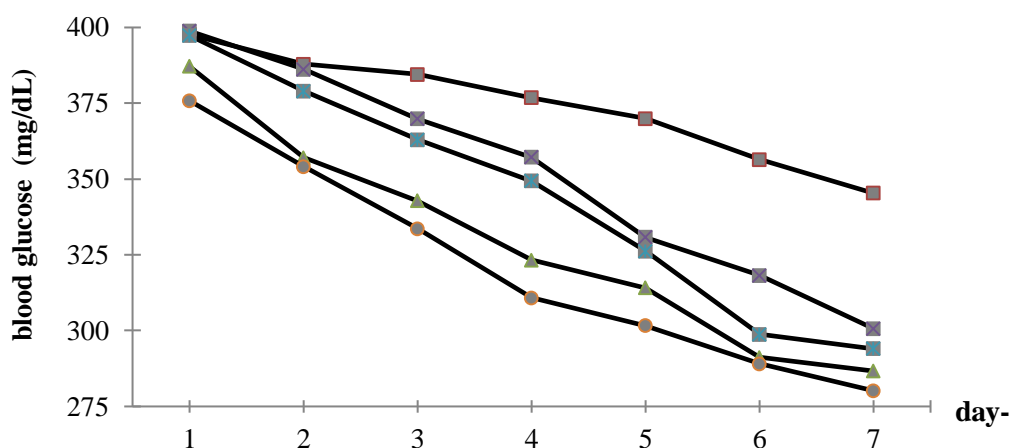
**Table II.** Comparison of Blood Glucose Level Before And After Alloxan Treatment

Group	Blood glucose level (mg/dL)	
	Before*	After**
Na-CMC 0,5% -	76 ± 11.14	312.5 ± 32.33
Dose 1 (10 mg/kg BW)	76 ± 10.12	338.00 ± 42.67
Dose 2 (20 mg/kg BW)	83.5 ± 14.27	348.17 ± 54.18
Dose 3 (40 mg/kg BW)	87 ± 6.97	349.67 ± 49.14
Glibenclamide 0.65 mg/kg BW <sup>+</sup>	75.33 ± 6.19	340.17 ± 25.97

\*before being induced using alloxan; \*\*after being induced using alloxan

-: negative control; +: positive control

The medication was administered orally once a day for 7 days to reduce the blood glucose levels (BGL) to normal limits ( $\leq 109$  mg/dL) (L. Wulandari, Nugraha, and Azhari 2020). The test preparation was administered to every group of diabetic mice on the first day (day 1). The test preparation was administered to each group of diabetic mice on the first day (day 1). According to the test results, the ethanolic extract of kedondong pagar leaves suspension at a dose of 10 mg/kg bw indicated a reduction in typical BGL to typical restricts on day 6, that a dosage of 20 mg/kg bw indicated a reduce in typical BGL to typical restricts on day 4, at a dosage of 40 mg/kg indicated a reduce in the mean BGL from mice to typical restricts on day 4, glibenclamide 0.65 mg/kg bw indicated a decrease in average BGL to normal inhibits on day 5, while use of Na-CMC 0.5% bb. Figure 2 depicts the consequences of decreasing the average BGL in mice.



**Figure 2.** The profile of mice groups blood glucose levels after treatment using kedondong pagar leaves (●: glibenclamide; ■: CMC-Na; ×: dose 1; \*: dose 2; and ▲: dose 3).

Based on the Figure 2, treatment about the ethanol extract from kedondong pagar leaves at doses of 10 mg/kg bw, 20 mg/kg bw, and 40 mg/kg bw did not significantly difference from the experimental group provided glibenclamide 0.65 mg/kg bw, while the untreated group CMC Na 0.5% bw did. Increasing the dosage increased the impact of lowering the BGL, although there was no significant difference between the treatment groups. This indicates that doses of 10 mg/kg bw, 20 mg/kg bw, and 40 mg/kg bw have the same capacity to reduce BGL in mice induced with alloxan. It showed that small dose (10mg/kg bw) of ethanol extract of kedondong pagar leaves already have antidiabetic on mice. Based on the conversion by Laurence and Bacharach (1964), the dose of 10 mg/kg BW in mice was the same as of that 3.879 g/kg BW in humans.

According to [Safriana et al. \(2021\)](#), kedondong pagar leaves include compounds known as flavonoids as antioxidants that make glucose absorption easier and faster into the blood, thereby stimulating pancreatic cells to produce insulin and decreasing blood glucose levels. Glycoside compounds, which have a benzene ring structure and a sugar group, are very reactive to hydroxyl radicals and thus act as hydroxyl radical scavengers ([Studiawan and Santosa 2005](#)). A decrease in blood glucose levels can also be caused by the presence of tannin compounds, which can increase the sensitivity of pancreatic  $\beta$ -cells to insulin release ([Hananti, Hidayat, and Yanti 2018](#)). These compounds can neutralize and prevent alloxan-induced free radical damage in normal pancreatic beta cells ([Atangwho et al. 2008](#)).

## CONCLUSION

The study's findings demonstrate that the ethanolic extract of kedondong pagar leaves has the capacity to lower blood glucose levels in mice caused by alloxan, implying that the ethanol extraction from kedondong pagar leaves has an antidiabetic effect.

## ACKNOWLEDGMENT

The authors would like to thank Kementerian Pendidikan, Kebudayaan, and Riset dan Teknologi for the 2021 Beginner Lecturer Research grant.

## REFERENCES

- Atangwho, IJ et al. 2008. "Effect of *Vernonia Amygdalina* Del. on Liver Function in Alloxan-Induced Hyperglycaemic Rats." *Journal of Pharmacy & Bioresources* 4(1).
- Brahmachari, Goutam. 2010. "Nevadensin: Isolation, Chemistry and Bioactivity." *International Journal of Green Pharmacy* 4(4).
- Datu, Ovie Syenni, Julianri Sari Lebang, and Elly Juliana Suoth. 2023. "Efek Pemberian Ekstrak Buah Salak (*Salacca Zalacca*) Dalam Menurunkan Kadar Glukosa Darah Pada Tikus Model Diabetes Melitus." *Jurnal MIPA* 12(1).
- Depkes RI. 2008. Farmakope Herbal Indonesia *Farmakope Herbal Indonesia*.
- Dewinta, Nena Ristra, Indri Safitri Mukono, and Arifa Mustika. 2020. "Pengaruh Pemberian Ekstrak Dandang Gendis (*Clinacanthus Nutans*) Terhadap Kadar Glukosa Darah Pada Tikus Wistar Model Diabetes Melitus." *Jurnal Medik Veteriner* 3(1).
- Hananti, Rina Sari, Saeful - Hidayat, and Lisma - Yanti. 2018. "UJI AKTIVITAS ANTIDIABETES EKSTRAK ETANOL KULIT KAYU MANIS (*Cinnamomum Burmannii* Nees Ex.Bl.) DIBANDINGKAN DENGAN GLIBENKLAMID PADA MENCIT JANTAN GALUR Swiss Webster DENGAN METODE TOLERANSI GLUKOSA." *Jurnal Sains dan Teknologi Farmasi Indonesia* 1(1).
- Krishnaraju, Alluri V et al. 2005. "Assessment of Bioactivity of Indian Medicinal Plants Using Brine Shrimp (*Artemia Salina*) Lethality Assay." *International Journal of Applied Science and Engineering Int. J. Appl. Sci. Eng* 3(2).
- Laurence, D.R., and A.L. Bacharach. 1964. "Evaluation of Drug Activities: Pharmacometrics." In *Academic Press*.
- Osinubi, Abraham Adewale, Glory O. Ajayi, and Elijah A. Adesuyan. 2005. "Abstract #752: Evaluation of the Antidiabetic Property of *Tapinanthus Butungii* Leaves in Rats with Alloxan-Induced Diabetes." *Endocrine Practice* 11.
- Ozougwu, Ozougwu. 2013. "The Pathogenesis and Pathophysiology of Type 1 and Type 2 Diabetes Mellitus." *Journal of Physiology and Pathophysiology* 4(4).
- Safriana, Safriana, Andilala Andilala, Cut Fatimah, and Samrani Samrani. 2021. "Profil Fitokimia Simplisia Dan Ekstrak Etanol Daun Kedondong Pagar (*Lansea Coromandelica* (Houtt.) Merr.) Sebagai Tanaman Obat." *Jurnal Ilmu Kefarmasian Indonesia* 19(2): 226.
- Studiawan, Herra, and Mulja Hadi Santosa. 2005. "Uji Aktivitas Penurun Kadar Glukosa Darah Ekstrak Daun *Eugenia Polyantha* Pada Mencit Yang Diinduksi Aloksan Metode Penelitian." *Media Kedokteran Hewan* 21(2).

- Triplitt, Curtis L, Thomas Repas, and Carlos Alvarez. 2017. "Chapter 74: Diabetes Mellitus." In *Pharmacotherapy A Pathophysiologic Approach Tenth Edition*,.
- Wijayakusuma, H. 2002. "Tumbuhan Berkhasiat Obat Indonesia Rempah, Rimpang Dan Umbi." *Prestasi Instan Indonesia, Jakarta*.
- Wulandari, Catharina Endah, Pudjadi, and Henny Kartikawati. 2010. "Pengaruh Pemberian Ekstrak Bawang Merah (*Allium Ascalonicum*) Terhadap Penurunan Kadar Glukosa Darah Pada Tikus Wistar Hiperglikemia." *Jurnal Universitas Diponegoro*.
- Wulandari, Lesty, Ari Satia Nugraha, and Nuri Putri Azhari. 2020. "Penentuan Aktivitas Antioksidan Dan Antidiabetes Ekstrak Daun Kepundung (*Baccaurea Racemosa* Muell.Arg.) Secara In Vitro." *Jurnal Sains Farmasi & Klinis* 7(1).