Potential of medang reso (*Cinnamomum parthenoxylon*) as raw material source for antidiabetic drugs

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Abstract. Diabetics is known as a dangerous comorbid disease in covid 19 patience. Many herbal medicines are used to prevent diabetes. Recently, the use of herbal medicine increased rapidly. In Indonesia, many indigenous plants have been used as source of raw material of herbal medicine including *Cinnamomum parthenoxylon*. Previous study reported that in vitro administration of *C. parthenoxylon* extract could reduce the sugar level and increased the plasma insulin level. Data on phytochemistry and bio-activity of this species are unavailable yet. Therefore, this study examined the phytochemical constituents and antidiabetic activity of their leaves. The leaves of *C. pathenoxylon* were collected from Bangka Belitung and South Sumatra for phytochemical screening and in vitro study. The phytochemical screening showed that constituents of flavonoids, steroids, tannins, alkaloids, and saponins were contained in the water extract of *C. pathenoxylon* leaves. The study indicated that extract leaves of *C. pathenoxylon* contains antidiabetic activity. In conclusion, *C. pathenoxylon* has the potential to be utilized as a source of raw material for diabetes medication. However, further in vivo and human administration studies are essentially required.

1. Introduction

Diabetes Mellitus (DM) is the source of various diseases, such as hypertension, heart disease, stroke, kidney failure, and blindness. DM is a syndrome characterized by hyperglycemia, changes in lipids metabolism, carbohydrates, and proteins, also potentially increase the risk of vascular disease complication [1]. Large numbers of world population suffer from diabetes. The International Diabetes Federation (IDF) in 2017 stated that more than 425 million people in the world, in the age range of 20-79 years old had diabetes and this number would continue growing [2]. Indonesia is ranked 4th in the world after India, China, and The United States of America for diabetes prevalence. WHO predicts DM type 2 patients in Indonesia would significantly increase reaching of 21.3 million people by the next 2030 [2].

Diabetes is a comorbid in covid-19 patients which contributed to the death of covid-19 patients. DM is comorbid with the highest death rate and it has the highest case (16.2%) in Indonesia [3]. The Indonesian Task Force of Acceleration in Covid-19 Handling mentioned that 34.8% cases of the comorbid diabetic (DM) are infected by covid [4].

Even though some antidiabetics are available commercially, some still show a side effect of adverse allergic reactions. Currently, back to nature campaign such as the use of herbal medicines is
being carried out by community. Since it is believed that herbal medicines have less severe side effects, less cost, and essentially alleviate the illness. The data of basic health research in 2010 showed that 59.12% of the Indonesian population are herbal medicine consumers, and about 95.60% have already felt the benefits [5]. The Research on medicinal plants then become concerned for finding new active compounds and bio-medicines ingredients.

Indonesia is rich of indigenous and endemic plants that has been used for traditional healing. *Cinnamomum parthenoxylon* (medang reso) is one of the species that has been used traditionally by local people to alleviate fever, hemorrhoids, flatulence, and wound infection. Phenotypically, *C. parthenoxylon* is a tree with height and diameter that can reach up to 45 m and 105 cm, respectively. It has a cylindric and straight trunk; bark with shallow groove and falls off in small flakes [6], grey silverish in color, and emits a nice fragrance. The leave is single, alternate, green with a brown-reddish tip, and nicely scented. The fruit is round, green while young and changes into blackish in color when it is ripe [7].

The previous study showed that in vitro administration of *C. parthenoxylon* extract was able to reduce sugar level and increase plasma insulin level [8]. However, data on phytochemicals and antidiabetic activity in the leaves of *C. parthenoxylon* is still considerably lacked. Therefore, this study was aimed to quantitatively examine the phytochemical constituents and antidiabetic activity of *C. parthenoxylon* leaves.

2. Materials and Methods

2.1. Sample Collection
Leaves sample were collected from the Island of Bangka Belitung, namely Air Menduyung and Terabek Village and from the forest area for special purposes (KHDTK) Kemampo, Kayu Ara Village, Banyuasin Regency, South Sumatra. Prior to further sample preparation, the leaves were cleaned to remove dirt and microbes.

2.2. Quantitative phytochemical screening
Phytochemical screening was done in the Biochemistry Laboratory, Medical Faculty, Lambung Mangkurat University (Banjarbaru City, South Kalimantan). Flavonoids, steroids, tannin, alkaloids, and saponins were examined. Total flavonoid was analyzed with the aluminum-chloride test using quercetin as the standard. Total steroid and saponin were analyzed with the method by [9]. Tannin content was determined with The Van-Burden and Robinson method. Alkaloid content was examined with the Harborne method.

2.3. Antidiabetic test
The antidiabetic test was carried out in the Biochemistry Laboratory, Medical Faculty of Lambung Mangkurat University, Banjarbaru City of South Kalimantan Province.

2.3.1. Test Method. Preparation of test solution (Au) = 1 mL Hb + 5 µL gentamicin + 1 ml glucose 2% (in 0.01 M phosphate buffer pH 7.4) + 25 µL leaves sample (30 µg/mL). Preparation of control solution (Ac) = 1 mL Hb + 5 µL gentamicin + 1 mL glucose 2% (in 0.01 M phosphate buffer pH 7.4) + 25 µL PBS pH 7.4. Preparation of standard solution (As) = 1 mL Hb + 5 µL gentamicin + 1 mL glucose 2% (in 0.01 M phosphate buffer pH 7.4) + 25 µL common antidiabetic medicine. The test solution, control, and standard solutions were incubated for 24 hours in a room temperature and dark condition. Of those solutions (Au, Ac, As), 10 µL was taken and diluted with 2 mL NaCl 0.9%. The absorbance was determined with spectrophotometer at wavelength (λ) 443 nm. The antidiabetic activity was calculated by comparing the result of Au with Ac and then multiplied with 100%.
3. Results and Discussion

3.1. Phytochemical constituents

The results showed that leaves extract of C. parthenoxylon from all locations contained all of the tested phytochemicals, i.e., flavonoids, steroids, tannins, alkaloids, and saponins (Table 1).

Table 1. Phytochemicals of water extract of the leaves of C. parthenoxylon from 3 sites.

| No. | Growing sites                     | Flavonoids (%) | Steroids (%) | Tannins (%) | Alkaloids (%) | Saponins (%) |
|-----|----------------------------------|----------------|--------------|-------------|---------------|--------------|
| 1   | Air Menduyung, West Bangka, Bangka Belitung | 8.57           | 0.91         | 0.63        | 0.58          | 0.47         |
| 2   | Terabek, West Bangka, Bangka Belitung     | 8.54           | 0.81         | 3.42        | 0.23          | 0.81         |
| 3   | Kemampo, Banyuasin, South Sumatera      | 11.09          | 0.88         | 0.68        | 1.75          | 0.67         |

The flavonoids content of C. parthenoxylon varied between sites, ranged from 8.57 to 11.09% (Table 1). The highest total flavonoid was observed in the Kemampo sample with 11.09%. The Kemampo sample also had the highest alkaloids content in comparison with two other locations with 1.75% of alkaloids content (Table 1). The C. parthenoxylon from Terabek sample exhibit the highest tannins and saponins content. Especially tannins from Terabek, it has 3.42% of content, differs significantly with the other sites (Table 1). Meanwhile, the C. parthenoxylon from Air Menduyung sample showed the highest steroids content with 0.91% (Table 1).

Those detected phytochemical constituents in the leaves of C. parthenoxylon show the potential of this plant as a medicinal plant. Those chemicals constituents have various therapeutic effects [10], such as antidiabetic, antihypertension, anticancer, anti-hypercholesterolemia [11], antioxidants, antiinflammation, antiulcer, antihepatotoxic, antibiotic [12]. This current study is in accordance with those previous studies [10-12].

3.2. Antidiabetic capacity

Leaves extract of C. parthenoxylon from all growing sites exhibited antidiabetic activity (Figure 1).

![Figure 1. Antidiabetic activity of water extract of C. parthenoxylon leaves.](image-url)

The leaves extract of C. parthenoxylon could reduce the occurrence of glycated hemoglobin formation; which is an indicator to control blood sugar. The addition of water extract of C. parthenoxylon leaves showed an inhibition activity on the glycated hemoglobin formation. Furthermore, water extract of sample from Kemampo even showed a higher potential of glycated hemoglobin inhibition compared to commercial antidiabetic medicine i.e., metformin. Metformin is an
oral medicine of DM to reduce the accumulation of glycated hemoglobin by inhibiting the formation of glycated hemoglobin [13] and inhibits cell necrosis of β-pancreatic and gluconeogenesis [14]. A decline in the glycated hemoglobin level indicates a controllable DM and reduces the risk of patients experiencing complications.

Previous studies found that glycated hemoglobin is related to blood sugar control and plays an important role in the occurrence of diabetic complications. A study found that an uncontrollable hyperglycemia condition occurred due to a high level of glycated hemoglobin [15]. The increase in glycated hemoglobin level indicated that an uncontrollable DM has high-risk potential of long-term complications on the patients e.g., retinopathy, neuropathy, nephropathy, and cardiopathy [16]. A high level of glycated hemoglobin increases diabetic retinopathy prevalence which is a microvascular complication of DM [17]. Meanwhile, a decrease of glycated hemoglobin by 1% would reduce the death risk caused by diabetes by 21%, heart attack by 14%, microvascular complications by 37%, and peripheral vascular disease by 43% [18].

The potential of water extract of C. parthenoxylon leaves as antidiabetic is due to the phytochemicals contained in the extract i.e., flavonoid, tannin, alkaloid, saponin, and steroid. Similar finding reported that ethanol extract of pirdot (Saurauia bracteosa) leaves contained flavonoid, steroid, saponin, tannin, and glycosides [19]. Some other studies also support this finding that those phytochemicals possess antidiabetic activity through several mechanisms [20]. Flavonoids, alkaloids, and polyphenols were potential as antidiabetic agents due to their capability to obstruct the formation of glycated hemoglobin [20]. Flavonoids could reduce the level of glucose and glycated hemoglobin in the streptozotocin-induced diabetic mice [21]. Plant alkaloids and flavonoids were potential as antidiabetic agents through the inhibition of the α-glucoside enzyme [22]. Flavonoids such as kaempferol and quercetin affect the β-pancreatic cell thus could enhance proliferation and insulin secretion [23]. The phytochemical constituent that is suggested to have antidiabetic activity in the water extract of C. parthenoxylon leaves is the flavonoid because it was observed as the highest quantitative level among other constituents.

4. Conclusion

Water extract of C. parthenoxylon leaves originated from the Island of Bangka Belitung and South Sumatra are potential as the source of raw material for antidiabetic medicine. The leaves extract contains phytochemical constituents i.e., flavonoids, steroids, tannins, alkaloids and saponins, and showed antidiabetic activity through the inhibition of glycated hemoglobin. Further examination is required to study the in vivo and clinical effects of C. parthenoxylon.

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