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REVIEW OF POTENTIAL PLANTS IN INDONESIA AS AN ANTIDIABETIC WITH HYPOGLYCEMIC ACTIVITIES

Mutiarani Dasha Hanggaresty [1*], Ni Kadek Warditiani[1]

[1]Departement of Pharmacy, Udayana University, Bali, Indonesia

Corresponding author email : kadektia@unud.ac.id

ABSTRACT

Background: Diabetes mellitus which is characterized by hyperglycemia, is a metabolic disease due to insulin action, defects in insulin secretion, or both. Various studies have shown that herbs that have a hypoglycemic effect can be used in the treatment of diabetes mellitus. Generally, herbs can slow down the complications of diabetes mellitus and improve metabolism. The ability of plants to restore the function of pancreatic tissue to increase insulin production or make it easier for insulin to process glucose is related to the effects of hypoglycemia. **Objective:** Comparing plants that have a hypoglycemic activity that can be used in the treatment of diabetes mellitus in Indonesia. **Methods:** studying literature from various databases, websites, national journals, and relevant international journals to identify plants that have hypoglycemic activity. **Results:** The mechanism *A. sativum* as a hypoglycemic involves different fiber viscosities; *A. vera* involved as a hypoglycemic by protecting pancreatic β cells; Asiatic acid in *C. asiatica* increasing glycolysis by restoring the activity of key enzymes; *G. max* inhibiting α-amylase and the stigmasterol increasing the absorption of blood glucose and reducing insulin resistance; *P. macrocarpa* exert their antidiabetic action via α-glucosidase modulation, an extra distinctive pancreatic mechanism; *S. arvensis* has the potential to inhibit α-amylase enzymes. **Conclusions:** This review article has presented 6 details of plants that have a hypoglycemic activity that can be used in the treatment of diabetes mellitus in Indonesia, and we believe it can be useful for students, researchers or practitioners.

Keywords: Diabetes mellitus, hypoglycemia, Indonesian plants

INTRODUCTION

According to the American Diabetes Association, diabetes characterized by hyperglycemia is a metabolic disease resulting from insulin action, lack of insulin secretion, or both[1]. Hyperglycemia for a long time can result in dysfunction and failure of organs, namely the kidneys, nerves, heart, eyes, and blood vessels. The prevalence of diabetes mellitus is increasing from year to year and Indonesia ranks fourth in the world with the highest number of sufferers of diabetes mellitus after India, China and America. WHO estimates that the number of sufferers in Indonesia will increase from 8.4 million in 2000 to 21.3 million in 2030[2]. In the province of Bali, the prevalence of diabetes mellitus diagnosed by health professionals and based on symptoms is 1.0%, whereas in Denpasar city, the provincial capital of Bali, the prevalence is 2.0%[3].

Various studies have shown that herbs that have a hypoglycemic effect can be used in therapy diabetes mellitus. The use of herbal medicines is supported by several factors. First, the side effects are lower than synthetic drugs because natural ingredients work through several mechanisms activated by several different

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chemical compounds. Second, it is safer because it works without the harmful properties of chemical excipients in synthetic drugs[4]. Generally, herbs can slow down the complications of diabetes mellitus and improve metabolism. The ability of plants to restore the function of pancreatic tissue to increase insulin production or make it easier for insulin to process glucose is related to the effects of hypoglycemia[5].

Indonesia has medicinal plants that have the potential to be antidiabetic. Some that are commonly used by the community are *Aloe vera*, *Allium sativum*, *Centella asiatica*, *Glycine max*, *Phaleria macrocarpa*, and *Sonchus arvensis*.

METHODOLOGY

The preparation of this article uses the method of studying literature from various databases, websites, national journals, and relevant international journals to identify plants that have activity as hypoglycemic. We searched through ScienceDirect, Medline, Google Scholar, and other popular sources. All articles or journals used is the last 10 years, the use of literature for more than 10 years is done if there are no other supported libraries. The literatures were read thoroughly and data extracted to present the 6 hypoglycemic plants below with reference to plant families, morphological descriptions, chemical content, and mechanisms as hypoglycemic. This plant can be used as an initial reference to find out potential hypoglycemic herbs and not definite or complete ones. We consider the original author's representations in all sources to be correct and based on evidence.

RESULTS AND DISCUSSION

Allium sativum L.

Family : Liliaceae[6]

Morphology :

Allium sativum bulb measures 1.5 - 3 inches in diameter depending on the variety and cultivar. *A. sativum* tubers have 4-60 chives (cloves) of various sizes and shapes wrapped in a thin white or purplish red membrane. *A. sativum* bulb is just under 10 inches to over 6 feet tall. *A. sativum* root is a fibrous root type[6].

Chemical Contents :

The main chemical content in *A. sativum* is Allicin (diallyl disulfide-oxide) and S-allyl cysteine sulfoxide (precursor allicin and garlic oil)[7]. In addition, according to the phytochemical screening carried out by Ibegbulem and Chikezie, chemical contents that also have a hypoglycemic effect are tannins, flavonoids, and alkaloids[8].

Mechanism as a hypoglycemic :

The mechanism of *A. sativum* can lower glucose levels which involves different fiber viscosities. First, plant fibers increase viscosity and block glucose diffusion, and second, they bind to glucose and decrease glucose transport across membranes. Although the exact mechanism by which *A. sativum* exerts its hypoglycemic activity is unknown. However, the ability of fiber *A. sativum* to inhibit absorption certainly has an important effect on carbohydrate metabolism[9].

Aloe vera

Family : Liliaceae[10]

Morphology :

Aloe vera has a single leaf that is 40–60 cm long, 2–3 cm wide, and 8–3 lower midrib 13 cm, greyish-green, boneless, and succulent at the top, which contains water, sap and mucus that dominates the leaves with a waxy coating. The top of the leaf is flat and the bottom is rounded (convex). The leaves have pale green or white spots and will disappear when the *A. vera* leaves are mature. The edges of the *A. vera* leaves are serrated and colorless[11].

Chemical Contents :

The main chemical content of *A. vera* gel are water and polysaccharides (pectin, hemicellulose, glucomannan, acemannan,and mannose derivatives). Aloe

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vera gel also contains lipid acids, amino acids, tannins, sterols (lupeol, campesterol, and sitosterols), and enzymes[12]. In addition, according to the phytochemical screening carried out by Raphael (2012), *A. vera* leaves contain alkaloids, tannins, flavonoids, carbohydrates, and terpenoids that can be used in medicine[13]. Meanwhile, according to Okamura et al. (1998), *A. vera* leaves contain phenols which can be divided into 2 groups, namely chromones (such as aloesin) and anthraquinones (such as aloin A and B)[14].

Mechanism as a hypoglycemic :

According to the research of Rajasekaran et al. (2004), oral administration of extract *A. vera* is carried out at concentrations of 200 and 300 mg/kgBW in normal fasting mice, glucose-containing oral mice, and induced diabetic rats streptozotocin (STZ). The research showed administration of *A. vera* significantly reduced blood glucose levels in glucose-containing animals. The remarkable increase in body weight along with a decrease in blood glucose levels in the *A. vera*-treated group of mice may be due to an increase in glucose metabolism by *A. vera*. It demonstrates the hypoglycemic activity of *A. vera* in diabetic rats. Thus, it can be seen that *A. vera* has hypoglycemic activity by maintaining glucose homeostasis during STZ-induced diabetes in mice by changing the activity of carbohydrate metabolism enzymes and protein metabolism.[10] According to research by Beppu et al. (2006), derivatives of anthrone or chromone of *A. vera* can be a component involved as a hypoglycemic by protecting pancreatic β cells from damage caused by free radicals from STZ that cause hyperglycemia[15].

Centella asiatica

Family : Umbelliferae[16]

Morphology :

Centella asiatica has the characteristics of creeping stems, chronic herbs, no stems, plant lengths ranging from 0.1–0.8 m, leaves in rosettes have a size of 2–0 10 per rosette, kidney shape, ridged edge 1–7 cm long, and 1–50 cm long petiole. *C. asiatica* has compound flowers in the form of umbrellas, the number of flowers is three per bouquet, and solitary or 2–5 bouquets[17].

Chemical Contents :

C. asiatica contains three active triterpenes, namely asiaticoside, madecassic acid, and asiatic acid[18]. In addition, *C. asiatica* also contains other active compounds such as phenolics, flavonoids (such as catechins, routine, naringin, quercetin, and luteolin), saponins, tannins, steroids, glycosides, sitosterol and stigmasterol from the steroid class, vallerin, brahmoside, brahminosides from saponins[19,20].

Mechanism as a hypoglycemic :

The effect of triterpenoids, which are the active substances of *C. asiatica*, is to reduce blood glucose levels in the body. In the research of Ramachandran and Saravanan (2013), asiatic acid acts as an antidiabetic by increasing glycolysis by restoring the activity of key enzymes such as glucose-6-phosphate dehydrogenase (G6PDH), hexokinase, and pyruvate kinase (PK)[21]. Research by Rice et al. (2010) showed that DM patients who have chronic hyperglycemia experience a decrease in the signaling pathway Phosphatidylinositide 3-Kinase (PI3K)/Akt required for insulin regulation[22]. Asiatic acid can increase insulin secretion by increasing the signaling Phosphatidylinositide 3-Kinase (PI3K)/Akt pathway[23]. In addition, these compounds also improve glucose response by increasing muscle GLUT-4 protein (Glucose Transporter Type 4), IR (Insulin Receptor), IRS-1 (Insulin-Receptor Substrate-1), and IRS 2 (Insulin-Receptor Substrate-2). Giving *C. asiatica* ethanol extract in the study of Palupi et al. (2019) succeeded in reducing the degree of insulitis which is also an indicator of pancreatic β cell repair[24].

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Glycine max

Family : Fabaceae[25]

Morphology :

Glycine max has a root structure consisting of two types, namely fiber roots and taproots, where the roots of these fibers grow from taproots. In addition, *G. max* can also form adventitious roots that grow from the bottom of the hypocotyl. *G. max* stems can grow up to 30-100 cm and *G. max* books in normal conditions range from 15-30 pieces[26]. *G. max* leaves can be round (oval) or taper (lanceolate). Differences in the shape of *G. max* leaves are influenced by genetic factors. Areas with high soil fertility are very suitable for *G. max* varieties that have wide leaf shapes[27]. *G. max* generally flowers between 5-7 weeks of age with leaf shape resembling a butterfly[26]. *G. max* seeds are between 6 - 30 g/ 100 seeds in pods, each pod containing 1–4 seeds with the shape of the seeds generally being round or round flat to oval[28].

Chemical content :

G. max contains protein, carbohydrates, fats, sterols and metabolite compounds such as flavonoids and isoflavones. Isoflavones are a subclass of flavonoid compounds that act as protective and preventive agents of plants. The isoflavone content in *G. max*, namely daidzein and genistein, is reported to have antioxidant and antidiabetic effects. Genistein acts as a specific inhibitor for α-glucosidase. *G. max* also contains minerals which include, K, P, Ca and Mg, various vitamins such as vitamin B, B12 and C and K [29,30]. Protein in *G. max*, especially glycine and arginine, has the effect of reducing insulin levels in the blood and is a diet for people with hyperglycemia, type 2 diabetes, hypertension, hyperlipidemia, athero-sclerosis and obesity. *G. max* contain fat which is mostly composed of triglycerides, sterols, phospholipids and non-saponified fats such as tocopherols and phytosterols[29]. 100 grams of *G. max* oil contains an average sterol of 300-400 mg. With details of the main sterol content, namely sitosterol (53-56%), cholesterol (20-23%), and stigmasterol (17-21%)[30].

Mechanism as a hypoglycemic :

According to McCue et al. (2005), extracts of *G. max* have potential hypoglycemic activity by inhibiting α-amylase and this activity can be increased by thermal processing (autoclaving) of *G. max* substrates, as well as through solid bioprocessing conditions with food fungi (*Rhizopus oligosporus* or *Lentinula edodes*) and by germinate in dark conditions[31]. In addition, the stigmasterol content in the study by Wang et al. (2017), can reducing excess blood sugar levels by increasing the absorption of blood glucose and reducing insulin resistance[32].

Phaleria macrocarpa

Family : Thymelaeaceae[33]

Morphology :

Phaleria macrocarpa has a tap root, round stem and sympodial branches that are greenish brown in color. *P. macrocarpa* has single leaves facing each other, pinnate leaves, lanceolate or oval-shaped leaf blades, tapered end and base bones, smooth surface, leaves 7-10 cm long and 3-5 cm wide. Flowers *P. macrocarpa* including compound interest spread in stems or axillary and are arranged in groups of 2-4 flowers without petals, tubular, and length of 1.5 to 2 cm. The crown of the god is in the form of an eclipse with a diameter of about 3 cm. The color of the fruit is green before ripe and red when ripe[17].

Chemical Contents :

P. macrocarpa contains mahkoside A, dodecanoic acid, palmitic acid, des-acetyl flavicordin-A, flavicordin-A, flavicordin-A glucoside, flavicordin-D, lignans and sucrose, and ethyl stearate[34]. The skin and fruits are rich in saponins, alkaloids, polyphenols, phenols, flavonoids, lignans and tannins. It contains kaempferol, naringin, myricetin, and rutin in the pericarp fruit.[35] Naringin and

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quercetin are found in mesocarp and seeds whereas phorboester and 29-norcucurbitacin have been isolated from seeds[35,36]. The fruits of *P. macrocarpa* contain icariside C3, phalerin, and mangiferin[37].

Mechanism as a hypoglycemic :

P. macrocarpa contains antidiabetic compounds namely, tannins, flavonoids and terpenoids which exert their antidiabetic action via α-glucosidase modulation, an extra distinctive pancreatic mechanism[38].

Sonchus arvensis

Family : Asteraceae[39]

Morphology :

Tempuyung leaves smell weak and taste slightly chelate, are single, stemless with lanceolate or oval-shaped, grooved fingers or irregular grooves, narrow or shaped leaf base arrows to a heart-shaped, irregular serrated leaf edge with a leaf length of 6 - 48 cm, a leaf width of 2 - 10 cm, the upper leaf surface is slightly coarse and paler in color[40].

Chemical Contents :

Various fractions of *S. arvensis* contain flavonoids and phenols, phytochemical analysis also reveals the presence of kaempferol, quercetin, orientin, routine, hyperoside, catechins, and myricetin[41]. Other studies have also reported that tempuyung leaf extract contains flavonoids and phenols[42,43].

Mechanism as a hypoglycemic :

The polyphenol content in extract *S. arvensis* as an antioxidant is reported to be able to suppress oxidative stress, which has a direct positive correlation to diabetes. There are three pathways for the emergence of oxidative stress, namely non-enzymatic protein glycation, the polio sorbitol pathway, and glucose autoxidation, where antioxidants are able to play a role in these three pathways, however, research data, especially clinical research, have not been consistent[44]. In vitro inhibition of α-amylase and α-glucosidase showed that *S. arvensis* made in infusion has the potential to inhibit α-amylase enzymes and the ability to inhibit-glucosidase enzymes is relatively small[45].

CONCLUSION

The review article above has presented 6 detailed of plants that have hypoglycemic activity that can be used in the treatment of diabetes mellitus in Indonesia. We believe that the plant details contained in this review can be useful for students, researchers or practitioners.

CONFLICT OF INTEREST

No conflict of interest in this paper. This paper was written independently without being affiliated by another party.

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