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Herbs Used as Antidiabetics : A Review

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ABSTRACT

Diabetes mellitus is a syndrome characterized by a condition of hyperglycemia, and changes in the metabolism of lipids, carbohydrates, and proteins. Diabetes mellitus is characterized by an increase in glucose levels caused by insulin deficiency either in absolute or relative terms. Diabetes mellitus therapy is a long-term therapy and is relatively expensive. Therefore, it is necessary to look for effective alternative drugs with low prices such as herbal medicines derived from plants. Indonesia is one of the countries that has a diversity of plants, so many plants that grow in Indonesia can be used as an alternative therapy to overcome diabetes mellitus. This paper aims to provide a relevant review of medicinal plants used for diabetes mellitus that has been carried out in research on tested animals. This research was conducted by searching for national and international articles from the internet, were searched from 2011 to 2019, including original articles, and experimental article, about Traditional medicine for diabetics. The following keywords are used : [["studi in vivo tumbuhan obat untuk diabetes" OR "Uji efektifitas ekstrak tumbuhan sebagai antidiabetik" OR "tumbuhan sebagai antidiabetik"]] OR [["Test extract activity against diabetic mice" OR "antidiabetic plant" OR "antidiabetic herbal medicine" OR "antidiabetic in rat", "Traditional medicine of diabetisin Indonesia"]]. From the results of the literature study, it was found that 21 articles with 24 medicinal plants were tested in vivo on test animals to reduce blood sugar in diabetes mellitus. These medicinal plants contain compounds of the type of flavonoids, alkaloids, tannins, saponins, polyphenols, terpenoids, and phenolics that can have a therapeutic effect on decreasing blood sugar levels in test animals.

KEYWORDS: *Herbal Plants, Antidiabetic Medicinal Plants, Flavonoids*

INTRODUCTION

Diabetes is one of the main diseases that has high morbidity and mortality rates worldwide. Diabetes mellitus is characterized by a condition of hyperglycemia, and changes in the metabolism of lipids, carbohydrates, and proteins. Increased glucose levels in diabetes mellitus can be caused by insulin deficiency either in absolute or relative terms. There are various factors that cause an increase in the prevalence of diabetes, such as population growth, old age, urbanization, obesity, and physical inactivity. The economic impact of diabetes with complications is quite large. According to the latest estimates, the prevalence of diabetes mellitus worldwide is 4%, this indicates that 143 million people with diabetes mellitus will increase to 300 million by 2025 (Dinesh et al., 2009).

Treatment of diabetes mellitus such as the use of insulin and oral antihiperglycemia drugs used over a long period of time. Therefore, it is necessary to look for effective drugs with low prices and relatively low side effects, namely herbal medicines derived from plants (Prameswari & Widjanarto, 2014).

Indonesia is a country that has a diversity of plants. The Asian continent has more than 70% medicinal plants which we can also find in Indonesia. However, not many of these medicinal plants are fully utilized by community. So, it is necessary to involve various parties to elevate the position of Indonesian medicinal plants, which have long been known, so that they can be aligned with modern medicine, and provide social and economic value to the Indonesian people (Lahamado et al, 2017). The use of medicinal plants for the treatment of diabetes mellitus is becoming common in the community. The use of these plants starts from with the belief of the people from generation to generation, which will then be proven by the results of scientific research (Lahamado et al, 2017).

Treatment of diseases using medicinal plants is in great demand by the public because the costs are cheaper when compared to synthetic raw materials or modern medicine (Fitriani, 2019).

Therefore, additional knowledge related to plants is needed that can be used for diabetes mellitus patients that have been through scientific tests. In this article we review medicinal plants used for diabetes mellitus that have been studied in test animals. This article providing information related to medicinal plants found around us that can be used as traditional medicine in the treatment of diabetes.

MATERIAL AND METHODS

This research was conducted by searching for national and international articles from the internet (google Schoolar and researchgate), were searched from 2011 to 2019, including original articles and experimental article, about Traditional medicine for diabetics. The following keywords are used : [["studi in vivo tumbuhan obat untuk diabetes" OR "Uji efektifitas ekstrak tumbuhan sebagai antidiabetik" OR "tumbuhan sebagai antidiabetik"]] OR [["Test extract activity against diabetic mice" OR "antidiabetic plant" OR "antidiabetic herbal medicine" OR "antidiabetic in rat", "Traditional medicine of diabetic in Indonesia"]]. Articles with duplicated records, and irrelevant full text were excluded.

RESULTS AND DISCUSSION

After conducting an initial search, selecting articles, removing duplicates and irrelevant records, 21 articles that were published between 2011 to 2019 were recruited. A total of 24 plants were tested on test animals. There are 3 articles that tested 2 different plants in 1 study. All articles collected are experimental, using test animals. Twelve studies compared medicinal herbs with antidiabetic drugs such as glibenclamide, 3 compared with metformin, and 1 with acarbose. Meanwhile, another study used a positive control with diabetic rats that had been induced with streptozocin and alloxan. Some 62.5% of the plant parts used as antidiabetics are leaves. While the rest is using fruit, rind, rhizome, and seeds. The study characteristics obtained are shown in table 1.

Table 1. Characteristics of research studies on Antidiabetic Medicinal Plants

Number	Writer	Publication Year	Plant Name	Ingredient Compound	Treatment		Outcome
					Blood sugar induction	Treatment	
1.	Fitriani *et al.*	2019	Groundcherry (*Physalis angulata*) and Gaharu leaves (*Aquilaria malaccensis*).	*Terpenoid*	Alloxan	Ethanol extract dosage: - 5 mg/kgBB of gaharu leaves and 50 mg/kgBW of groundcherry leaves - Gaharu leaves 10 mg / kgBW and groundcherry leaves 100 mg / kgBW Negative control: - Aquadest Positive control: - - Glibenclamide	Gaharu leaves at a dose of 10 mg/kBBg and groundcherry leaves (Physalis angulata) at a dose of 100 mg/kgBW are effective doses that have the effect of decreasing fasting blood sugar levels in male Wistar rats (Rattus norvegicus) with p-value <0.05
2.	Bisala *et al.*	2019	Taro Leaves (*Colosacia esculenta*)	*flavonoids, alkaloids, tannins, saponins and polyphenols.*	Streptozotocin	Ethanol extract dosage: - 100 mg / kgBW - 200 mg / kgBW - 400 mg / kgBW Negative control: - Na-CMC 0.5% Positive control: - - Metformin suspension	The ethanol extract of taro leaves has an antidiabetic effect with an effective dose of 200 mg/kg BW
3.	Bindu	2018	Ginger Rhizome (*Zingiber officinale*)	*Fenol*	Streptozotocin	Ethanol extract dosage: - 500 mg / kgBW Negative control: - - Diabetic rat	The results showed that raw ginger has the potential for hypoglycemic, hypocholesterolemic, and hypolipidemic. Additionally, raw ginger was effective in reversing the diabetic proteinuria observed in diabetic rats.
4.	Fitriani, *et al.*	2017	Combination of Bitter leaf (*Vernonia amygdalina*)and Green chiretta leaf (*Andrographis paniculata*)	*Alkaloids, tannins, saponins, flavonoids, polyphenols, and vitamin C*	Alloxan	Combination extract of bitter leaf and green chiretta - Green chiretta 500 mg / kgBW and - Biiter leaf 100 mg/kg BW - KSA 1000/200 mg / kg BW - KSA 2000/400 mg / kg BW Negative control: - DM + Aquadest Positive control: DM + Acarbose	The combination of the ethanol extract of green chiretta leaf and the ethanol extract of Bitter leaf at a dose of 2000/400 mg/kg BW is effective in decreasing blood sugar levels with a value of p <0.05.

5.	Sasmita, *et al*.	2017	Tithonia diversifolia leaves	*Flavonoid and sesquiterpenes*	Alloxan	Tithonia diversifolia leaves extract: - - The extract dose 1,28 ml/200 gr BW - - The extract dose is 2,57 ml/200 gr BW - - Extract dose of ,14 ml/200 gr BB Negative control: - Without treatment Positive control: - - Treatment-induced only 2 ml alloxan	Tithonia diversifolia leaves have an antidiabetic effect or act as an antihyperglycemic at a dose of 5,14 ml/200 gr BW
6.	Theresia, *et al*.	2017	Surian Bark and Leaves (*Toona sinensi*)	*Flavonoids and terpenoids* (Nurdin et al, 2016). *Flavonoids, triterpenoids and tannins* (Monisa, 2016).	Streptozotocin	The dosage of ethanol extract of Surian bark and leaves : - 150 mg / kg BW - 300 mg / kg BW Negative control: - Mice induced by STZ Positive control: - - Glibenklamide	The dose that can reduce blood glucose levels is 150 mg/kgBW and is able to maintain the body weight of the rats by 17.7% and 25.3%.
7.	Wahyuni	2017	Meniran Leaves (*Phyllanthus niruri L.)*	*Flavonoid*	Alloxan	Control group: - Without giving the extract Ex. Treatment: - - Given meniran extract 5.0 mg / kg BW / day	Meniran leaf extract with a dose of 5.0 mg/kg BW / day can repair pancreatic-cell damage and decrease blood glucose levels.
8.	Lahamado *et al*.	2017	Tamarind Leaves (*Tamarindus indica L.*)	*Flavonoid, tanin, glikosida, saponin.*	EDTA	The dosage of tamarind ethanol extract: - 10% - 20% - 40% Negative control: - Na-CMC 1% Positive control: - - Glibenclamide	The test results on animals at a significant level of 5% showed that 40% tamarind extract had an effect on decreasing blood sugar levels in rats.
9.	Sundhani, *et al*.	2016	Syzygium campanulatum korth leaf and Rhoeo discolar leaf	*Flavonoid, ascorbic acid, alkaloid, saponin, terpenoid* (Sitorus et al, 2012)	Glucose	-Rhoeo discolor leaf ethanol extract doses of 100, 200, 400 mg / kg BW -Ethanol extract of Syzygium campanulatum korth leaf with doses of 300, 600, and 1200 mg / kg BW. - Negative control: - CMC Na solution - Positive control: - Glibenclamide 0.6 mg / kgBW	The combination of the ethanol extract of Rhoeo discolor leaf with doses of 200 and 400 mg/kg BW and Syzygium campanulatum korth leaf at doses of 300 and 600 mg/kg BW can decrease blood sugar levels equivalent to the provision of glibenclamide 0.6 mg/kg BW.
10.	Lukiati	2016	Chayote (*Sechium edule*)	*Polyphenols, and flavonoid.*	Streptozotocin	Chayote ethanol extract: - The extract dosage is 14 mg / kg BW	Chayote ethanol extract dose of 42 mg / kg BW can decrease blood

				(Aini et al, 2014)		- The extract dosage is 28 mg / kg BW - The extract dosage is 42 mg / kg BW Negative control: - Healthy mice Positive control: - DM mice induced by STZ	sugar levels with a value of p <0.01.
11.	Anas	2015	Lenglengan leaf (*Leucas lavandulifolia JE. Smith*)	*Aecetin, chryosoeriol, limfoside,chryosoeriol-6-(Oac)-4-β-glukosida, lupeol* and *tarakseron.*	Exogenous insulin	- The dosage of lenglengan leaf ethanol extract: - - 62.5 mg / kgBW/ day - - 125 mg / kgBW / day - - 250 mg / kgBW / day - Negative control: - - Na-CMC 0.5% 12.5 ml / kg BW/ day - Positive control: - - Metformin 150 mg / kg BW / day	On the three treatments of the extract dosage for 14 days was proven to have an antidiabetic effect of type 2 in diabetic rats with insulin resistance.
12.	Gushiken et al,	2016	Neem Leaves (*Azadirachta indica*)	*Flavonoids, triterpenoid,* and *glycosides.*	Alloxan	Dosage of neem leaf ethanol extract: - 100 mg / kgBW / day - 250 mg / kgBW / day Negative control: - Aquadest Positive control: - - Glibenclamide	In the glucose tolerance test in diabetic rats with neem extract 250 mg / kg showed significantly lower glucose levels compared to the control group.
13.	Syafmir, *et al*.	2014	Jengkol bark (*Archidendron pauciflorum (BENTH.) I.C. NIELSEN*).	*Flavonoid, alkaloid, tanin, quinones,* and *polyphenols.*	Alloxan	The dosage ethanol extract of jengkol bark - 500 mg / kg BW - 1 gr / kg BW - 1.5 gr / kg BW Negative control: - Induced + PGA 3% Positive control: - - Glibenklamide	The ethanol extract of jengkol bark at a dose of 1.5 g / kg BW has the same antidiabetic activity as the comparator for glibenklamide at a dose of 0.09 mg / 200 g BW.
14.	Muhammed *et al*.	2014	Black cumin seed oil (*Nigella sativa L.*)	*Saponins, alkaloids, essential oils.*	Streptozotocin	Dosage extract of black cumin seed oil: - 100 mg / kgBW - 200 mg / kgBW - 300 mg / kgBW Negative control: - Na-CMC Positive control: - - Glibenclamide	The provision of 300 mg/kg BW of black cumin seed oil extract has been shown to have antidiabetic effects.
15.	Prameswari.	2014	Pandan leaf (*Pandanus amaryllifolius, Roxb*).	*Tanin, alkaloid, flavonoid,* and *polyphenols*	Alloxan	Pandan leaf water extract dosage: - 300 mg / kgBW - 600 mg / kgBW Negative control: - Mice induced alloxan Positive control: - - Metformin	The results showed that the water extract dose of Pandan leaves of 600 mg / kgBW was better in decreasing blood glucose levels and repairing pancreatic tissue when compared to the dose of 300 mg / kgBW.

16.	Alamoudi *et al.*	2014	Pacing rhizome (*Costus speciosus*)	*Flavonoid*	Streptozotocin	Pacing ethanol extract dosage: - 50 mg / kgBW / day - 100mg / kgBW / day - 150mg / kgBW / day Negative control: - Oral saline (C) Positive control: - Mice injected with STZ	The extract dose of 150 mg/kg body weight has the potential to cause it antidiabetic activity by inhibiting hepatic glucose.
17.	Kaempe, *et al.*	2013	Goroho Banana (*Musa spp*)	*Phenolic, tannins, flavonoids.*	Alloxan	Goroho banana extract: - Fresh extract - Banana flour extract - Kalamansi extract Negative control: - Alloksan Positive control: - Glibenclamide	The highest extract of Goroho banana that could decrease blood sugar levels in the rats was fresh banana extract at 67.6 mg / dl (61.19%) with a p value <0.05.
18.	Cahyanto *et al.*	2013	Tabat Barito (*Ficus deltoidea jack*)	*Phenols* and *saponins*	Glucose	Barito-ethanol extract dosage: - 50 mg / kgBW - 100 mg / kgBW - 200 mg / kgBW Negative control: - Glucose Positive control - - Glibenclamide	Blood glucose levels of rats given a dose of 50-200 kg / BW extract ranged from 132.60-258.00 mg / dL, glibenclamide ranged from 130.20-144.60 mg / dL. The percentage decrease in blood sugar levels compared to controls was 32.54%
19.	Yuda *et al*	2013	Bitter Melon (*Momordica charantia*)	*Flavonoid, saponin,* and *polyphenols.*	Alloxan	Bitter melon ethanol extract dosage: - 100mg / kgBW - 50 mg / kgBW Negative control: - Rats without treatment Positive control: - Glibenclamide 1 mg / kgBW	The results showed that the ethanol extract of bitter melon at a dose ratio of 100 and 50 mg / kg BW, both of them were stated to reduce blood sugar levels. However, at a dose of 100 mg / kg BW has an effect comparable to glibenclamide in lowering blood sugar.
20.	Faridah baroroh *et al.*	2011	Gardenia Leaves (*Gardenia augusta, Merr*)	*Saponins, flavonoids, crocetin polyphenols, crocin,* and *scandosida.*	Glucose	Dosage ethanol extract of Gardenia leaves - 500 mg / kgBW - 250 mg / kgBW Negative control: - Glucose Positive control: - Glibenclamide	The dosage ethanol extract of gardenia leaf which can reduce blood sugar levels is 500 mg / kgBW and 250 mg / kgBW.
21	Wehantouw, *et al.*	2011	Mangosteen rind (*Garcinia mangostana L.*)	*Flavonoids, tannins, triterpenoid,* and *saponins.*	Sucrose	Mangosteen peel extract dosage: - 1.25 gr / BW Negative control: - Aquadest Positive control: - Glibenclamide	The test results showed that the mangosteen peel extract showed antidiabetic activity against sucrose-induced rats for 4 hours.

The content of medicinal plant compounds for the treatment of diabetes mellitus

Based on the results of literature studies, it is known that the most chemical compounds in medicinal plants used to treat diabetes are flavonoids, followed by saponins, tannins, polyphenols, terpenoids and alkaloids. The content of the dominant chemical compounds in medicinal plants used for diabetes mellitus can be seen in Figure 1.

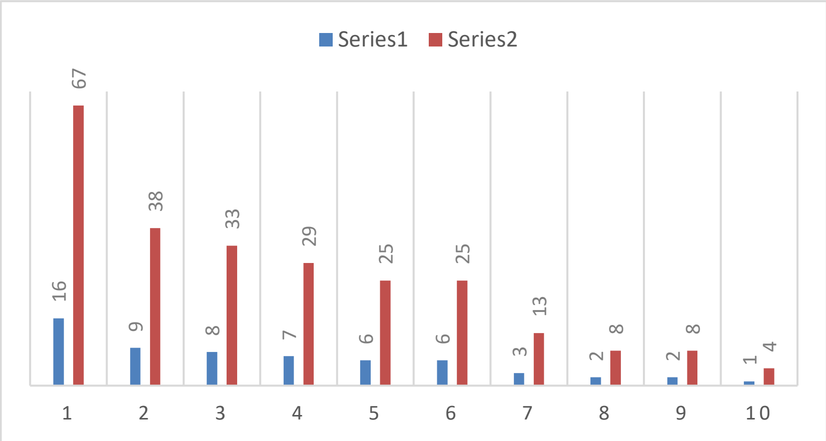

Figure 1. Compound Content in Medicinal Plants

Diabetes affects many metabolic pathways in human tissue, some of which are potential targets for treatment. Most of the studies on antidiabetic herbs have focused on in vitro analysis. However, this approach is difficult in identifying new treatments because most in vitro test models only consider single cell types, metabolic pathways or enzymes; thus greatly reducing the possibility of identifying an extract or compound plant antidiabetic. So in this case, animal models are more appropriate for evaluating the antidiabetic properties of medicinal plants (Afolayan & Sunmonu, 2010).

Based on the data in the table above, it can be seen that there are 24 medicinal plants that are efficacious for antidiabetic therapy that were tested using test animals. These plants contain hypoglycemic compounds that can reduce glucose levels in the blood at different doses (Afolayan & Sunmonu, 2010).

In the test process, the test animals commonly used as experimental animals are white rats. In a study, test animals were divided into several treatment groups to see if there were differences in results, namely the positive control group, the negative control group and the testing group (Baroroh et al, 2011). Before the experiment is carried out, the test animal must be conditioned with diabetes by various induction methods. Induction of diabetes is usually done using alloxan. Alloxan is a diabetogenic substance that is toxic, especially to pancreatic beta cells and if given to experimental animals it can cause diabetes (Prameswari and Widjanarko, 2014).

Alloxan is used for diabetes induction because it is toxic if given to test animals by damaging pancreatic beta cells. The mechanism of damage to pancreatic beta cells by alloxan begins with the oxidation of sulfhydryl groups and the formation of free radicals. Alloxan reacts with two groups –SH that binds to the side of the protein or amino acid and forms a disulfide bond so that it activates the protein which results in disruption of the protein function. Alloxan induction at a dose of 125 mg / Kg BW intraperitoneally was able to increase glucose levels in rats so that they reached a state of hyperglycemia with blood glucose levels> 135 mg / Dl. Alloxan is an unstable hydrophilic compound. Alloxan can reach the pancreas very quickly and its action begins with the rapid uptake by Langerhans beta cells. The formation of reactive oxygen begins with the reduction of alloxan in Langerhans beta cells. Alloxan also has high activity in cellular compounds containing SH groups, reduced glutathione (GSH), cysteine and protein-bound sulfhydryl compounds. The result of the alloxan reduction process is dialuric acid, which then undergoes reoxidation to become alloxan (Prameswari & Widjanarko, 2014).

In addition to using alloxan, induction of experimental animals to become diabetic can also use streptozosin (STZ). STZ is often used as the induction of insulin-dependent and induction of non-insulin-dependent diabetes in test animals used because it can damage the pancreatic beta cells by working directly on the pancreatic beta cells by the action cytotoxic which is mediated by reactive oxygen species (ROS) and can be used as an induction of diabetes mellitus. STZ as a diabetonic agent can trigger an increase in the production of excess free radicals and cause oxidative stress, then measure blood glucose levels after induction to see the increase, after which the mice are treated according to the specified group. Streptozotosin (STZ) is obtained from Streptomyces achromogenes, which can be used to induce DM type 1 and DM type 2 in test animals. STZ penetrates langerhans beta cells via the glucose transporter GLUT 2. The intracellular action of STZ results in DNA changes in pancreatic beta cells. STZ can inhibit the krebs cycle and decrease mitochondrial oxygen consumption. Limited mitochondrial ATP production can result in a drastic reduction in pancreatic beta cell nucleotides (Bisala, 2019)

As a comparison, drugs that have a mechanism of action to stimulate insulin secretion are used. Trials of diabetes mellitus using test animals are based on the pathogenesis of the disease in humans. Research using tested animals has found a variety of diagnoses, therapies, drugs, and medicinal plants that can be used to treat diabetes mellitus. However, the pathological conditions in test animals are not completely similar to those in humans. This is due to pathological differences between several models of diabetes mellitus, differences in physiological conditions, the presence of complications that accompany the disease, and the variety of diabetes mellitus (Baroroh et al, 2011).

In table 1, it can be seen that from the research that has been done, the drug

In figure 1 it is stated that the most chemical compounds contained in medicinal plants used to treat diabetes mellitus are flavonoids, followed by saponins, polyphenols, tannins, terpenoids, and alkaloids. These compounds can overcome

a. Flavonoids

Flavonoids have a C-Aryl glucoside group that inhibits SGLT (Sodium-Glucose Contransporter Inhibitors) which works by breaking glycoside bonds in SGLT. In general, flavonoids stimulate enzymes found in humans. The α-glucosidase enzyme works by breaking down carbohydrates, helping carbohydrate absorption and increasing insulin sensitivity. Aldose reductase enzymes, break down glucose in polyol pathways. PPAR-g Enzymes it Help to regulate fatty acid and glucose metabolism. Meniran leaves are an example of plants that contain flavonoids (Sangeetha et al., 2016).

Flavonoids are group of natural phenolic compounds found in plants, which are composed of 15 carbon atoms as their basic nucleus. Composed of a C6-C3 - C6 configuration, namely 2 aromatic rings

glibenclamide is the most widely used as a positive control. The mechanism of action of glibenclamide in reducing blood sugar levels is by stimulating insulin release by inhibiting the attachment of urea sulfonyl receptors in Langhears Island β cells. In the end, it can cause the opening of calcium channel tension, which can trigger an increase in intra-cell calcium β (Akash, 2013).

free radicals and prevent toxic compounds in the body. In addition, some of these plants also have an antidiabetic function that can lower blood glucose levels so that they can prevent diabetes and can be used as therapy for those with diabetes.

connected by three carbon atoms, which can or cannot form a third ring, as in the following figure.

b. Saponin

Apart from flavonoids, alkaloids, and tannins, saponins can also lower blood sugar by inhibiting the action of the a-glucosidase enzyme. The a-glucosidase enzyme is an enzyme found in the intestine that has the function of converting carbohydrates into glucose. This enzyme inhibits glucose absorption in the small intestine, so that it can decrease glucose levels in the blood. Saponins have an effect on the arrangement of the cell membrane that can inhibit molecular absorption and can cause disruption in the glucose transporter system, thereby inhibiting glucose absorption. Plants that contain saponin compounds include black cumin and tamarind (Fiana et al, 2016)

c. Tanins

While tannin has a role in stimulating glucose and fat metabolism, so that the accumulation of these substances in the blood can be avoided. It also has hypoglycemic activity, tannins can also shrink the epithelial membrane in the small intestine so that the absorbed food juices and sugar intake can be inhibited. This keeps blood sugar level from rising too high. Goroho banana and mangosteen peel are examples of plants that contain tannin compounds (Dewanti et al, 2019).

d. Polyphenols

Polyphenols have a role in lowering blood sugar levels. Polyphenols work by preventing the reaction of converting superoxide to hydrogen superoxide. The role of polyphenols is the protection of pancreatic β-cells from the toxic effects produced by free radicals and produced during chronic hyperglycemia conditions. Polyphenol can be defined as a chemical compound that generally contains natural ingredients where the basic structure has an aromatic group that is attached to one or more OH groups. One of the plants containing polyphenolic compounds is chayote (Dewanti et al, 2019).

e. Terpenoids

Terpenoids are dehydrogenated and oxygenated derivatives of terpenes. Terpenes are a group of hydrocarbons that are mostly produced by plants and some animal groups. Terpenoids contained in groundcherry and gaharu leaves also have antidiabetic activity where the mechanism of action is to stimulate the release of insulin and help glucose absorption by stimulating GLUT-4 in cells. The word terpenoid includes a large number of plant compounds and this term is used to indicate that biosynthetically, all plant compounds come from the same compound but this does not mean that there are similarities in function or chemical properties. All terpenoids originate from the Isoprene molecule CH2 = C (CH3) -CH = CH2 and the carbon framework is constructed by joining two or more C5 units (Elza Sundhani et al, 2016).

f. Alkaloids

The next compound is alkaloids. It shown to have the ability to regenerate. The alkaloid extracts have been shown to have the ability to regenerate damaged β-cells of the pancreas. Alkaloids can also stimulate the sympathetic nerves (sympathomimetics) which can have an effect on increasing insulin secretion. To lower blood sugar, alkaloids work by increasing glucose transport in the blood, inhibiting glucose absorption in the intestine, stimulating glycogen synthesis and inhibiting glucose synthesis by inhibiting the glucose 6-phosphatase enzyme. Inhibition of the 6-phosphatase enzyme will reduce the formation of glucose from substrates other than carbohydrates. Plants that contain alkaloid compounds include jengkol bark and fragrant pandan leaves (Miten et al, 2014).

g. Phenolic

The phenolics found in tabar barito and ginger can also reduce blood glucose levels. Phenolics works by inhibiting gluconeogenesis. Gluconeogenesis is inhibited by suppressing the phospohoenolpyruvate carboxykinase (PEPCK) enzyme through increasing adenosine monophospate activated protein kinase (AMPK) in the liver (Isdamayani, 2015).

CONCLUSION

In Indonesia, cases of diabetes mellitus continue to increase every year. Therefore, the use of medicinal plants can provide a good alternative. The use of medicinal plants to treat diabetes mellitus has been empirically tested by the public. From the various types of plants in Indonesia that can be used as traditional anti-diabetic medicines, there are 24 herbal plants documented in the scientific literature that have shown anti-diabetic activity. Of the twenty-four plants, most of them contain flavonoids, terpenoids, tannins, saponins, and phenolic compounds that can play a role in decreasing blood sugar in test animals.

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