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A MINI REVIEW ON ZINGIBERACEAE FAMILY AS ANTIDIABETIC PLANTS: ACTIVE INGREDIENTS AND MECHANISMS OF ACTIONS

Fatiya Zata Ishmah[1*], Agus Sulaeman[2]
[1]*Master of Pharmacy Study Program, Faculty of Pharmacy, Bhakti Kencana University Bandung, 40614*
[2] *Department of Pharmacology and Clinical Pharmacy, Faculty of Pharmacy, Bhakti Kencana University Bandung, 40614*
**Email Corresponding: fatiyazataishmah@gmail.com*

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ABSTRACT

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia that occurs due to abnormalities in insulin secretion. Therapy using conventional anti-diabetic drugs is associated with serious side effects, and herbs to maintain chronic disease if conventional drugs not adequate. The purpose of this article review is to find out information about plants of the *Zingiberaceae* family that have anti-diabetic activity with the mechanism of action of α -glucosidase enzyme inhibition, α -amylase enzyme inhibition, and increased GLP-1 levels. The sources used consisted of 27 journals and reviewed 9 research journals originating from Google Scholar, Pubmed, NCBI, Elsevier, Science Direct with a span of under 10 years. The articles were then analyzed using the systematic literature review method, by collecting, evaluating, and developing research on a particular topic. From several studies conducted, the results showed that plants from the family that have antidiabetic activity include *Zingiber officinale* (ginger), *Curcuma longa* (turmeric rhizome), *Curcuma aeruginosa* (temu hitam), *Curcuma zanthorrhiza* (curcuma), *Zingiber cassumunar* (bangle), *Kaempferia galanga* (kencur), *Alpinia galanga* (lengkuas), *Etlingera elatior* (kecombrang, honje), and *Elettaria cardamomum* (kapulaga).

Keywords: Antidiabetic; Diabetes Mellitus; Zingiberaceae

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia (increased glucose levels in the blood) that occurs due to defects in insulin secretion, insulin action, or both (PERKENI, 2021). From the 2018 RISKESDAS (Basic Health Research) results, it appears that the prevalence of DM patients in Indonesia is still increasing. Not only that, but the number of prediabetic patients is still quite high. Impaired fasting blood glucose as much as 26.3% and impaired glucose tolerance as much as 30.8% of the entire population who do TTGO (oral glucose tolerance test). Based on DiabCare research data from 2016, only about 30% of type 2 DM patients undergoing treatment at health facilities with a 7% HbA1c. Uncontrolled DM will cause both microvascular and macrovascular complications that are difficult to manage. Every DM patient who already has micro- or macrovascular complications will cause a large social and financial burden for the country. Catastrophic diseases are still a concern in the implementation of the JKN-KIS Program. Moreover, in 2020, BPJS Kesehatan has spent Rp. 20 trillion to pay for services and medicines for catastrophic diseases, one of which is diabetes mellitus (DM). The majority of DM disease was suffered by JKN-KIS participants whose age ranged from 51 to 65 years old, with a case prevalence of 57% of the total cases from 2017-2020. Diabetes cases continue to increase from year to year. To provide services to participants, especially

those with DM, BPJS Kesehatan has collaborated with 22,965 First Level Health Facilities (FKTP) and 2,567 hospitals (BPJS, 2021).

The global prevalence of diabetes mellitus in 2021 was 9.1% (464 million) and is projected to increase to 10.0% (638 million) in 2045. The global prevalence of diabetes mellitus in 2022 was 5.8% (298 million) and is projected to increase to 6.5% (414 million) in 2045. In 2022, the prevalence of diabetes mellitus was highest in high-income countries. In 2045, the largest relative growth in cases of diabetes mellitus will be in low-income countries. The global burden of prediabetes is substantial and growing. Enhancing prediabetes surveillance is necessary to effectively implement diabetes prevention policies and interventions (American Diabetes Association, 2023).

Death in diabetics is caused by acute and chronic complications. Acute complications include hyperglycemia and hypoglycemia, while chronic complications include: stroke and heart disease, neuropathy (damage to nerves that causes diabetic feet and amputations), retinopathy (damage to small blood vessels in the retina that causes cataracts and blindness), and the main cause of kidney failure. Regarding cardiovascular complications, DM sufferers are at risk of experiencing these complications two times more than non-DM patients (Kementerian Kesehatan RI., 2020). Diabetes is a leading cause of microvascular complications, such as nephropathy and retinopathy. It is also associated with an accelerating 66.5% of chronic macrovascular complications, consisting of coronary heart disease (33%), cerebrovascular disease (18.8%) and peripheral vascular disease (30%). A systematic review notes that cardiovascular disease is found in 32.2% of people with diabetes and is the main cause of death in 9.9% of patients with type 2 diabetes. Other sources note that, compared to adults without DM, adults with DM are 2-4 times more at risk of dying from cardiovascular complications (Rahmasari et al., 2020).

Glucose swallowed triggers a much greater insulin response than if it is administered intravenously. This effect, known as the incretin effect, is mediated by two hormones, namely glucagon-like polypeptide-1 (GLP-1) and glucose-dependent insulinotrophic polypeptide, also called gastric inhibitory polypeptide (GIP). In patients with type 2 DM, GLP-1 deficiency and resistance to the hormone GIP hormone. Incretin hormone is also immediately broken down by the presence of the DPP-4 enzyme, so it only works for a few minutes. Drugs that inhibit performance are DPP-4 inhibitors. The gastrointestinal tract also plays a role in the absorption of carbohydrates through the performance of the enzyme α-glucosidase which breaks down polysaccharides into monosaccharides, and then absorbed by the intestine, resulting in an increase in blood glucose after meals. Drugs that inhibit the performance of the α- glucosidase enzyme are acarbose.When carbohydrates enter the colon, they are still in the form of polysaccharides, which are then changed into monosaccharides by the enzyme α-glucosidase. monosaccharides that the liver will convert to glucose. Due to an increase in the amount of food that has entered the intestines, there are more people who have diabetes as a result of a rise in glucose induced by the amount of carbs. Acarbose is one medication that inhibits the α-glucosidase enzyme as a result, preventing a rise (PERKENI, 2021).

Decreased amylin production in diabetes is a consequence of pancreatic beta cell damage. Decreased amylin levels lead to accelerated gastric emptying and increased absorption of glucose in the small intestine, which is associated with increased postprandial glucose levels.

Dipeptidyl peptidase-4 (DPP-4) is a serine protease, that is widely distributed in the body. This enzyme cleaves two amino acids from peptides containing either alanine or proline at the second position of the peptide's N-terminus. DPP-4 enzymes are expressed in various organs, including the intestine and renal brush border membranes, hepatocytes, the vascular endothelium of capillary villi, and in a soluble form in plasma. DPP-4 inhibitors will inhibit the binding site on DPP-4 so that it will prevent the inactivation of glucagon-like peptide (GLP)-1. This inhibition process will maintain GLP-1 and glucose-dependent insulinotropic polypeptide (GIP) levels in an active form in the blood circulation, thereby improving glucose tolerance, increasing insulin response, and reducing glucagon secretion.

DPP-4 inhibitors are oral agents, and those included in this group are vildagliptin, linagliptin, sitagliptin, saxagliptin, and alogliptin.

Treatment of DM can be done by administering antidiabetic and non-pharmacological drugs. Pharmacological therapy uses antidiabetic drugs, one of which is the α-glucosidase inhibitor agents that are often used clinically, namely acarbose and miglitol, but these two drugs have side effects and can cause other diseases if they are not appropriate and there is no adherence to treatment. Thus, the use of natural medicine at this time as an alternative therapy is more considered because of its potential and minimal side effects (DiPiro et al., 2016).

Efforts that can be made to manage type II diabetes mellitus include non-pharmacological therapy and pharmacological therapy. Non-pharmacological therapy can be done by modifying lifestyle, while pharmacological therapy can be done through the use of oral anti-diabetic drugs. One of the drugs that can be used to treat type II diabetes mellitus is acarbose. Acarbose works by inhibiting the action of enzymes α-glucosidase. The α-glucosidase enzyme is an important enzyme that plays a role in the hydrolysis of carbohydrates into glucose. Inhibition of this enzyme will have an impact on delayed glucose absorption (Khatri & Juvekar, 2014). Long-term us of synthetic antidiabetic drugs such as deep acarbose can cause some side effects such as interference with the digestive tract such as nausea, vomiting, stomach pain, and bloating (DiNicolantonio et al., 2015). Natural medicine is therefore more widely regarded as an alternative therapy due to its potential and few side effects. (Nakhaee & Sanjari, 2013).

From previous studies, it is known that [6]-gingerol stimulates GLP-1- mediated insulin secretion pathway, upregulate *Rab27a/Slp4*, controls the exocytosis of insulin granules in the pancreatic β-cells, and facilitates glucose disposal in skeletal muscle by regulating glycogen synthase 1 and by increasing GLUT4 membrane presentation (Samad, 2017).

α-glucosidase inhibitors inhibit the absorption of carbohydrates from the small intestine. They competitively inhibit enzymes that convert complex, non-absorbable carbohydrates into simple absorbable carbohydrates. These enzymes include glucoamylase, sucrase, maltase, and isomaltase. By delaying carbohydrate absorption, they reduce the rise in postprandial blood glucose concentrations by about 3 mmol/L (Derosa & Maffioli, 2012), (Kumar et al., 2011)

Acarbose is the most commonly used drug in this class and also the most widely studied one. Others include voglibose and miglitol. Acarbose inhibits α-amylase, maltase, sucrase, and dextranase and is most effective against glucoamylase. It does not affect lactase, which is a beta-glucosidase. Acarbose and voglibose (not FDA-approved in the USA) are poorly absorbed from the gut, have low bioavailability, and are excreted in the stool. Miglitol, on the other hand, is absorbed from the gut completely and is excreted through the renal route. Acarbose undergoes metabolism in the colon, while miglitol and voglibose have no metabolites (Göke B. et al., 1995).

α-Amylase, a salivary or pancreatic enzyme, plays an important role in the early breakdown of complex carbohydrates into simple molecules. Modulation of α-amylase activity affects the utilization of carbohydrates as an energy source, and stronger is this modulation, more significant is the reduction in the breakdown of complex carbohydrates. Majority of studies have focused on antiamylase phenolic compounds. Inhibition of α-amylase, enzyme that plays a role in digestion of starch and glycogen, is considered a strategy for the treatment of disorders in the carbohydrate uptake, such as diabetes and obesity, as well as; dental caries and periodontal diseases (de Sales et al., 2012).

In recent years, the incretin system has become an important target in the treatment of type 2 diabetes, and glucagon-like peptide 1 (GLP-1) is of particular interest for its glucose-lowering effects. The physiological response to oral ingestion of nutrients, involving the incretin system, is reduced in some patients with type 2 diabetes but may be augmented by administration of GLP-1 receptor agonists. The GLP-1 receptor agonists currently approved in the United States for the treatment of type 2 diabetes include exenatide

(administered twice daily), liraglutide and lixisenatide (administered once daily), and the once-weekly agents exenatide extended-release, albiglutide, and dulaglutide. These agents have been shown to reduce A1C (by 0.8–1.6%), body weight (by 1–3 kg), blood pressure, and lipids. GLP-1 receptor agonists are associated with a low risk of hypoglycemia, and the most common adverse effects are gastrointestinal. Proper patient selection and education can assist in achieving positive treatment outcomes (Andersen et al., 2022).

To obtain metabolites from the crude, it is necessary to extract according to the nature of the active substance and the solvent that matches the solubility of the active substance. Identification of active compounds as secondary metabolites using appropriate tools. Isolation of secondary metabolite compounds from a natural material can be carried out with various extraction methods, namely Soxhlet, maceration, and percolation. Secondary metabolite compounds contained in natural materials can dissolve in solvents with different polarity properties. Which have different polarity properties. Polar compounds dissolve in polar solvents, while non-polar compounds dissolve in non-polar solvents, so that the solvent used will selectively separate the compound content (Zhang et al., 2018).

RESEARCH METHOD

This article review was created with the aim of providing information about herbal medicine as an alternative derived from several plants that have antidiabetic activity with various mechanisms of action. Finding suitable α-glucosidase and α amylase inhibitors with minimal side effects is the demand of the day, and it is respectfully challenge to know efficacious antidiabetic drugs with minimal or no adverse effects. In order to deal with this problem effectively, WHO has recommended exploration and development of a safer and better antidiabetic than nature, especially from plants (WHO, 2014). Taking this history into account, traditional anti-diabetic plants were selected to finish this study.

This study uses a literature review study, with analytical steps to find and combine several abstracts and analyze facts from various scientific sources that match valid and accurate criteria. The literature review presents a summary in the form of the most relevant publications, then compares the results presented in the papers. The data sources used in this article consist of primary and tertiary sources. The primary data source in this article is in the form of scientific journals, both national and international. Meanwhile, tertiary sources are trusted websites such as Google Scholar, PubMed, NCBI, Elsevier, Science Direct, and others. The inclusion criteria used in this journal are national and international scientific journals (2014-2022). The keywords used were Zingberaceae, antidiabetic, diabetes mellitus, α-glucosidase enzyme inhibition, α-amylase so the results obtained were 27 journals and 9 research journals reviewed. The analysis was carried out using the systematic literature review method, which examined, identified, studied, and evaluated the results and discussion so that research could be developed on a particular focus.

RESULTS AND DISCUSSION

Zingiberaceae Plants

Plants from the Zingiberaceae family consist of *Zingiber officinale* (ginger), *Curcuma longa* (turmeric rhizome), *Curcuma aeruginosa* (temu hitam), *Curcuma xanthorrhiza* (curcuma), *Zingiber cassumunar* (bangle), *Kaempferia galanga* (galangal), *Alpinia galanga* (galangal), *Etlingera elatior* (kecombrang, honje), and *Elettaria cardamomum* (Cardamom).

Zingiberaceae is one of the many plants found in tropical forest areas, especially Indo-Malaya. The Zingiberaceae family is found in about 50 percent of tropical forests (Pandey, 2003). Zingiberaceae can live from the lowlands to an altitude of more than 2000 meters above sea level, especially in areas with high rainfall. So far, the areas rich in Zingiberaceae are the Malesiana region, Indonesia, Brunei, Singapore, the Philippines, and Papua. We know that large areas such as Sumatra and Borneo are still very unknown and are being investigated more deeply for their ginger flora. Therefore, many new types will certainly be discovered in the coming year (Saensouk et al., 2022).

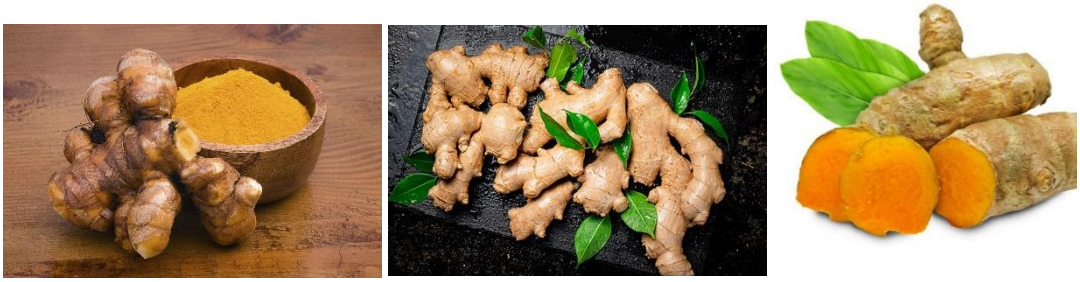
Zingiberaceae, also known as the ginger family, is the largest family of the order Zingiberales, it is divided into about 53 genera and made up of more than 1300 species. These aromatic flowering plants are widely distributed throughout the tropics and subtropics; and are especially abundant in Southeast Asia. Many species belonging to the ginger family have been widely used as spices or flavoring agents; due to their aromatic odors and, pungent and spicy taste. Galangal, one of the most well-known ginger-like spices of the Zingiberaceae family, was frequently used in Southeast Asia for culinary and medicinal purposes. It is a highly pungent and aromatic rhizome related to common ginger but with a personality distinctly its own. Galangal, or its variant galanga, usually refers to two plant species of the ginger family (John Kress et al., 2002). Traditional medicines that can be used as inhibitors of the α-glucosidase enzyme include turmeric, ginger (Hasan et al., 2022), bangle (Yuniarto and Selifiana, 2018), kapulaga (Sh Ahmed et al., 2017), kecombrang (Nor et al., 2020), temulawak (Nurcholis et al., 2018), kencur (Kokila et al., 2020), and lengkuas (Verma et al., 2015).

According to (Daily et al., (2015) and; (Riaz et al., (2015), ginger (*Zingiber officinale* Rosc.) as an antidiabetic because it contains phytochemical components that can inhibit the α-glucosidase enzyme. Gingerol, zingeron, and other flavonoid derivatives are ingredients that can inhibit the α-glucosidase enzyme (Yanto et al., 2016). Cardamom (*Elettaria cardamomum*) is a plant species that belongs to the Zingiberaceae, or ginger family (Nurcholis et al., 2018).

Turmeric contains active polyphenolic compounds such as curcuminoids, essential oils, and turmerone phenylpropane derivatives (Simorangkir, 2020). Turmeric functions as an antidiabetic by inhibiting the mechanism of the α-glucosidase enzyme (Nurdin et al., 2017). Turmeric functions as an antidiabetic by inhibiting the mechanism of the α-glucosidase enzyme (Hasimun et al., 2016).

An alternative for treating diabetes mellitus is herbal medicine, which is made from plants. To avoid the negative effects of traditional anti-diabetic medications, herbal medicine is used. It has been demonstrated that certain plants, when extracted at specific concentrations, exhibit anti-diabetic properties. *Alpinia galanga*, *Elettaria cardamom*, and *Kaempferia galanga* are used by the community as spices and medicines, while *Curcuma longa* is used as a cooking spice, a herbal ingredient, and a medicine. Zingiber is used by the community as a medicine, seasoning, beverage ingredient, and in traditional rituals. These plants were harvested from yards, gardens, and rice fields, as well as from wild species (Mutaqin et al., 2017).

(a) (b) (c)



(d) (e) (f)

(g) (h)

Figure 1. The appearance of *Zingiberaceae* plant parts; (a) *Alpinia galanga* rhizomes; (b) *Elettaria cardamom* seeds (c) *Kaempferia galanga* rhizomes; (d) *Curcuma longa* rhizomes (e) *Zingiber officinale* rhizomes; (f) *Curcuma zanthorrhiza* rhizomes; (g) *Zingiber cassumunar* rhizomes; (h) *Etlingera elatior* flower

Based on several studies, the *Zingiberaceae* family has antidiabetic activity with various mechanisms of action, which can be seen in Table 1. Some methods that can be used to determine antidiabetic activity are inhibition of α-glucosidase enzyme, inhibition of the amylase enzyme, and an increase in GLP-1 levels.

Table I. List of *Zingiberaceae* Plants as Antidiabetics

No	Title	Author	Method	Induction	Results
1	In vitro antidiabetic and inhibitory potential of turmeric (*Curcuma longa* L) rhizome against cellular and LDL oxidation and angiotensin converting enzyme	(Lekshmi et al., 2014)	1. Inhibition of the α-glucosidase enzyme 2. Inhibition of α-amylase enzymes	-	1. The IC_{50} 0,4 µg/mL 2. The IC_{50} 71,6 µg/mL
2	Anti-diabetic activity of a methanolic extract of *Alpinia galanga* Linn. aerial parts in	(Verma et al., 2015)	Single intraperitoneal induction of streptozotocin (STZ) at a dose of 60 mg/kg body weight in to the rats tested.		reducing fasting blood glucose levels and reducing rat

	streptozotocin induced diabetic rats				body weight
3	[6]-Gingerol, from Zingiber officinale, potentiates GLP-1-mediated glucose-stimulated insulin secretion pathway in pancreatic β-cells and increases RAB8/ RAB10-regulated membrane presentation of GLUT4 transporters in skeletal muscle to improve hyperglycemia in Leprdb/db type 2 diabetic mice	(Samad, 2017)	• Each rat was given [6]- gingerol, Saxagliptin, negative control, positive control (Extendin), [6]- gingerol + Extendin, [6]- gingerol + Saxagliptin • Then anesthetized • The pancreas is taken, then incubated • Measured levels of GLP-1 and insulin in plasma		**Increasing** GLP-1 levels and insulin Levels
4	Evaluation of in vitro antidiabetic and antioxidant characterizations of *Elettaria cardamomum* (L.) Maton (*Zingiberaceae*), *Piper cubeba* L. f. (*Piperaceae*), and *Plumeria rubra* L. (*Apocynaceae*)	(Sh Ahmed et al., 2017)	1. Inhibition of the α-glucosidase enzyme 2. Inhibition of α-amylase enzymes	-	1. % Inhibition 13,73 2. % Inhibition 39,93
5	Xanthorrhizol contents, α-glucosidase inhibition, and cytotoxic activities in the ethyl acetate fraction of *Curcuma xanthorrhiza* accessions from Indonesia	(Nurcholis et al., 2018)	Inhibition of the α-glucosidase enzyme	-	The IC_{50} value of α-glucosidase enzyme inhibitory activity has a range 339.05 mcg/mL – 445.01 mcg/mL
6	α-glucosidase Enzyme Inhibitory Activity of Bangle Rhizome Extract (*Zingiber cassumunar* Roxb.) In vitro	(Yuniarto & Selifiana, 2018)	Inhibition of the α-glucosidase enzyme	-	The IC_{50} 98.31 µg/mL
7	Evaluation of the antidiabetic activities of *Etlingera elatior* flower aqueous extract in vitro and in vivo	(Nor et al., 2020)	α-glucosidase enzyme inhibition α-amylase enzyme inhibition	Induction of 7 groups of mice (35 rats) with high-fat food for 6 weeks.	52.39 % (currently) 99.97 % (very high) Lowering blood sugar levels
8	Effect of *Kaempferia galanga* Rhizome Extract on Haematological Parameters in Streptozotocin-Induced Diabetic Wistar Rats	(Kokila et al., 2020)	Rats from 6 groups were induced and then given extracts and allowed to stand. After that measured serum	Induction of Streptozotocin dose of 60mg/kg BW and Dextrose 10% each	Lowering glucose serum

			glucose for 28 days.		
9	α-Glucosidase Inhibition Test from a Combination of Turmeric Extract, Black Tea and Ginger	(Hasan et al., 2022)	Inhibition of α-glucosidase	-	The IC50 66.64 mcg/mL

From the research table above, the drug used as a comparison is acarbose, where acarbose has a mechanism of action, namely inhibition of α-glucosidase enzymes and inhibition of α-amylase enzymes. while for drug comparators that have a mechanism of increased GLP-1 levels, namely alogliptin, sitagliptin, and linagliptin. These drugs will be compared with several plants from the Zingberaceae family, as described in the paragraphs below. Acarbose will be compared with *Curcuma longa*, *Elettaria cardamomum*, *Curcuma xanthorrhiza*, *Zingiber cassumunar*, *Etlingera elatior*, and *Zingiber officinale*. Sitagliptin will be compared with *Alpinia galanga*, *Zingiber officinale*, and *Kaempferia galanga*.

Turmeric (Curcuma longa)

Inhibition of glucosidase leads to an increase in PHg which is one of the diabetes-related risks factors. Glucosidase inhibitors play a major role in managing PHg in diabetic patients. In the studies, turmeric extract was screened for its inhibition activity against the enzymes α-glucosidase and α-amylase and the results are given in Table. 1. Ethyl acetate, methanol, and aqueous extract inhibited α-glucosidase activity in a dose-dependent manner with IC_{50} values of 0.4; 3.1 and 12.6 µg/mL, respectively. IC_{50} values were obtained for α-amylase inhibition potential of ethyl acetate, methanol, and water extracts were 71.6, 90.3, and 498.3 µg/mL, respectively. Under experimental conditions, standard glucosidase inhibiting acarbose drugs inhibit α-glucosidase and α-amylase enzymes with IC_{50} values of 17.1 and 290.6 µg/mL respectively. Ethyl acetate extract has the highest α-glucosidase and α-amylase inhibitory potential among extract. The glucose inhibitory potential of both ethyl acetates and methanol extract is significantly ($p<0.05$) higher than that of acarbose (Lekshmi et al., 2014). while the extract with the lowest IC_{50} value was obtained from turmeric extract with an average of 9.48±0.05µg/mL. Results of analysis of variance (ANOVA) turmeric extract has a lower IC_{50} value compared to the extracts of black tea and ginger significantly ($p<0.05$). Given that the IC_{50} value extracts black tea, turmeric, ginger, and acarbose significantly ($p<0.05$), then the follow-up test (Duncan) is done. The results of Duncan's test with a significance level of 5% indicated that the tea extracts of black, turmeric, and ginger were significantly different from acarbose, while black tea extract was not significantly different from turmeric extract. The best extract, is turmeric extract with the lowest IC_{50} value compared to other extracts, while ginger extract is considered the extract with the lowest activity (Hasan et al., 2022).

In the human intestine, inhibition of α-glucosidase was effective in delaying glucose absorption and preventing elevation of the postprandial blood glucose level; thus, α-glucosidase inhibitors are used as a glycemic control in the treatment of diabetes (Sivasothy et al., 2016). This report investigated the inhibitory activities of four *C. zanthorrhiza* accessions against α-glucosidase and the Cursina-III variety used as a control. The IC_{50} values of α-glucosidase inhibitory activities ranged from 339.05 ± 38.54 µg/ml to 455.01 ± 33.48 µg/ml. The ethyl acetate (EA) fraction from Karanganyar accession exhibited a higher α-glucosidase inhibitory activity (the lowest IC_{50} value) with a significantly in $p \leq 0.05$, while the EA fraction from Ngawi accession showed the weakest activity (the highest IC50 value). All the rhizome samples had less α-glucosidase inhibitor activity with an IC_{50} value of >200 µg/ml. Therefore, the EA fraction of *C. zanthorrhiza* accessions and the Cursina-III variety were not potential sources for α-glucosidase inhibitor active compounds (Nurcholis et al., 2018).

Kencur/sand ginger (Kaempferia galanga)

The research on *Kaempferia galanga* revealed a significant decrease in body weight in diabetic test animals compared to the controls group. Treatment of diabetic rats with hydroethanol *K. galanga* extract significantly improves body weight. Increased blood glucose levels reported by diabetic rats returned to near normal levels in the treated group, ensuring the potency of *K. galanga* in the management of obesity and hyperglycemia. Hematological studies revealed significant changes in RBC, WBC, PCV, and Hb levels in the treatment group compared with the diabetes group, and showed the hematoprotective effect of the hydroethanolic extract of *K. galanga* rhizome (Kokila et al., 2020).

Lengkuas (Alpinia galanga)

Methanolic extract of *A. galanga* aerial parts administered in 200 mg/kg and 400 mg/kg dose levels to STZ treated diabetic rats showed a significant reduction in blood glucose levels, which are related to the duration of treatment. The maximum reduction in blood glucose was observed after the 4^{th} day at dose 400 mg/kg body weight and after the 15th day at a dose of 200 mg/kg body weight. At the end of the study, the extract at dose 200 of and 400 mg/kg of body weight showed a significant reduction in blood sugar level in comparison with that of the diabetic control group. The body weight of rats increases normally when the test or standard doses are given to them in comparison to the control rats (Verma et al., 2015).

Ginger (Zingiber officinale)

In subsequent research, it was shown that [6]-Gingerol increases glucose-stimulated insulin secretion by activating the GLP-1-mediated insulin secretion pathway, regulates insulin granule exocytosis, and enhances glucose uptake in skeletal muscle by increasing membrane expression of GLUT4. How 6-Gingerol in increase plasma GLP-1 levels to give the observed results of insulin secretagogue activity remains unanswered. One possible mechanism for increasing plasma GLP-1 half-life is counter-acting dipeptidyl peptidase-4 (DPP4), which is known to cleave and in turn disable GLP-1 (Samad, 2017).

Kapulaga (Elettaria cardamomum)

The percentage inhibition of α-glucosidase by water extracts of *Elettaria cardamomum was* 10.41 (0.03), whereas the percentage inhibition by methanol extract was 13.73 (0.02). The percentage of α-amylase inhibition by aqueous extracts was 82.99 (0.01), while the percentage of inhibition by methanol extract was 39.93 (0.01). Water extract showed good in vitro antidiabetic and antioxidant activity. In addition, in vitro optimization experiments helped increase the inhibitory activity of α-glucosidase *E. cardamomum*. The findings of this study justify traditional claims. This plant is used as a traditional medicine for managing diabetes, however, through its inhibitory effects on digestive enzymes (Sh Ahmed et al., 2017).

Bangle (Zingiber cassumunar)

Then, in subsequent studies, the results of testing the activity of inhibition of the ethanol extract of bangle rhizome against the α -glucosidase enzyme in vitro were shown. The IC_{50} value obtained from the inhibitory activity of bangle rhizome extract against the α-glucosidase enzyme was 98.31 µg/ml. In this study, the standard drug used as a positive control was acarbose. The IC_{50} value of acarbose is 36.17 µg/ml. Based on the research results, the ethanol extract of bangle rhizome has the ability to inhibit enzyme activity α-glucosidase in vitro (Yuniarto & Selifiana, 2018). Chemical content of plants such as the presence of alkaloids, flavonoids, tannins, saponins, quinones, and steroids/triterpenoids is likely to have responsibility for α-glucosidase inhibitory activity. The highest IC_{50} value from research on ginger was obtained from ginger extract, with an average of 66.64 ± 0.44 µg/ml. Acarbose, as a comparison, has an IC50 value of 7.17 × 10-3 ± 0.00 µg/mL. (Hasan et al., 2022).

Kecombrang (Etlingera elatior)

Initial screening of *Etlingera elatior* flower aqueous extract (EEAE) for antidiabetic in vitro activity was carried out at 100 µg/ml extract. In this study, acarbose, a comparator inhibitors for α-amylase, and quercetin, well-known compounds to control postprandial hyperglycemia, were used as positive control drugs. Acarbose blocks pancreatic α-amylase and membrane-bound α-glucosidase, reducing the rate of carbohydrate digestion. Meanwhile, quercetin was used as a positive control for the α-glucosidase test based on reports claiming that phenolic compounds have stronger inhibitory activity α-glucosidase compared to acarbose (Indrianingsih et al., 2015). EEAE has strong inhibitory activity to the α-amylase enzyme, and there was no significant difference observed when compared with the positive control, acarbose. The results also showed that the EEAE showed 99.7 ± 4.97% of enzyme inhibition, whereas 100 ± 1.92% inhibition was achieved for acarbose. For the α-glucosidase test, EEAE showed moderate inhibition (52.39 ± 2.12%) and wasstatistically significant with quercetin compound (97.62 ± 1.23%) used as a positive control ($p<0.001$). Note that in this test, acarbose (10.62 ± 11.03%) showed weak inhibition of the α-glucosidase enzyme, and EEAE inhibitory activity was significantly higher than acarbose but lower than quercetin (Nor et al., 2020).

CONCLUSION

Plants of the Zingiberaceae family have anti-diabetic activity with the mechanism of action of α-glucosidase enzyme inhibition, α-amylase enzyme inhibition, and increased GLP-1 levels. Therapeutic intervention via inhibition of the enzyme α-glucosidase is a well-known strategy used for the treatment and management of type 2 diabetes. Acarbose, miglitol, and voglibose have become drugs with a mechanism of action of α-glucosidase inhibitors, which have been available commercially for the last three decades. Further research is needed to find effective ways to reduce toxicity. Plant compounds from natural sources of bioactive compounds can be used for the development of drugs that are effective against diabetes mellitus. This review article identified nine diverse plants that exhibit potent α-glucosidase inhibitory activity. The amount of information available on the selected compounds varies greatly, but before The studied molecules were all found to show various biological activities.

Collectively, based on what is presented, promising plants and compounds described in this review could be major drug candidates for future designs of new compounds useful in the management of type-2 diabetes treatment.

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