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Literature Review

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Indonesian medicinal plants as potential candidates for alpha-glucosidase inhibitor: A comprehensive literature review for anti-diabetic therapy

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Abstract: Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels due to impaired insulin activity. One therapeutic strategy to manage postprandial hyperglycaemia is the inhibition of the α-glucosidase enzyme, which plays a key role in carbohydrate digestion. This literature review aimed to identify Indonesian medicinal plants with potential α-glucosidase inhibitory activity based on in vitro studies. Articles were systematically retrieved from Google Scholar using specific keywords, covering publications from the last ten years (2014–2024) in English or Indonesian and accessible in full text. Inclusion criteria focused on studies evaluating in vitro α-glucosidase inhibition from Indonesian plant extracts; non-Indonesian or non-in vitro studies were excluded. Of the 200 screened articles, 34 fulfilled the eligibility criteria. Most studies employed spectrophotometric colorimetric assays using p-nitrophenyl-α-D-glucopyranoside (pNPG) as the substrate to assess inhibitory activity. In total, 40 plant species were identified as having α-glucosidase inhibitory potential, with active compounds primarily including flavonoids, polyphenols, alkaloids, saponins, and tannins. The most commonly observed mechanism was competitive inhibition, wherein active compounds, especially flavonoids, blocked carbohydrate hydrolysis and reduced glucose absorption. Some studies also reported mixed and non-competitive inhibition through allosteric binding or conformational changes in the enzyme. This review supports the potential of various Indonesian medicinal plants as sources of natural α-glucosidase inhibitors, highlighting their relevance for the development of safer, plant-based antidiabetic therapies.

Keywords: Alpha-glucosidase; Diabetes mellitus; In Vitro; Medicinal plants; Hyperglycemia.

INTRODUCTION

Diabetes mellitus (DM) is defined as a metabolic disorder caused by impaired insulin secretion in the pancreas, which prevents cells from absorbing glucose and utilizing it as an energy source.[1] The insulin hormone produced by the

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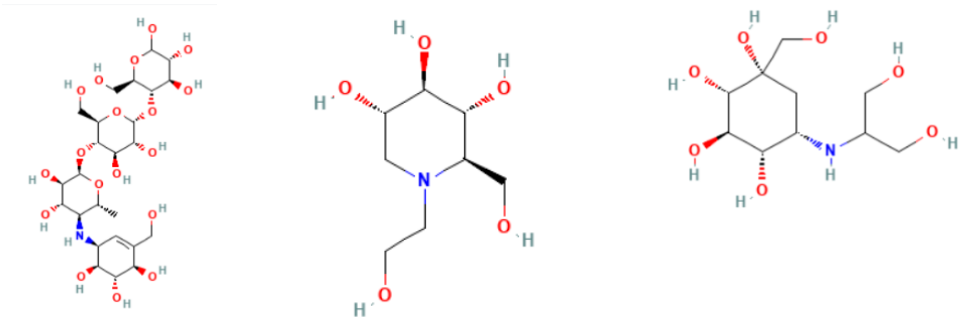
pancreas helps control blood sugar levels. In some diabetic patients, insulin cannot be processed in the pancreas, so that cells cannot absorb glucose and use it as energy in the body. [1] DM poses a global health threat due to its often asymptomatic nature until complications arise. According to the World Health Organization (WHO), the number of people with diabetes mellitus in Indonesia is projected to increase significantly, reaching 21.3 million by 2030.[2] In 2021, Indonesia ranked third in diabetes mellitus prevalence at 10,8% and placed seventh among the ten countries with the highest number of diabetes cases worldwide.[3] One of the therapeutic approaches to DM is by inhibiting the α-glucosidase enzyme that works in the carbohydrate digestion process, catalyzing the reaction of disaccharides to monosaccharides in the small intestine. The activity of this enzyme can slow down the absorption of glucose into the bloodstream, so that in the process of inhibition of the α-glucosidase enzyme, it has a significant impact on controlling blood sugar levels so that it can minimize postprandial blood sugar levels as a controller of hyperglycemia.[4] Alpha-glucosidase inhibitors are non-invasive treatments that generally have mild gastrointestinal side effects, which are short-term depending on the dose, such as diarrhea, abdominal pain, and bloating.[1] There are three α-glucosidase inhibitors used, including acarbose, miglitol, and voglibose (Figure 1).



Acarbose Miglitol Voglibose

Figure 1. Structure of Acarbose, Miglitol, and Voglibose (PubChem)

α-glucosidase enzyme inhibitor agents are available in Indonesia, one of which is acarbose, an oligosaccharide complex that functions to inhibit a number of enzymes involved in the process of breaking down complex carbohydrates in the intestine. Acarbose is able to inhibit membrane-bound α-glucosidase and pancreatic α-amylase, which function in the metabolism of complex starches and oligo-, tri, and disaccharides that will be absorbed into simple sugars.[5] That has prompted the search for safer alternatives through the screening of naturally occurring active compounds from plants.

Herbal plants remain a key component in drug development research. Indonesia's vast natural resources have encouraged the use of traditional medicine as an alternative treatment. Medicinal plants contain secondary metabolites that contribute to pharmacological activities, including antidiabetic effects.[6] Herbal medicine is often chosen to minimize the side effects of chemical therapies and support physiological functions. This review offers novelty by focusing specifically on studies from the past ten years that investigate the alpha-glucosidase inhibitory activity of Indonesian medicinal plants through in vitro assays, an area that has not been extensively reviewed. Therefore, this article highlights the importance of exploring Indonesian herbal plants as potential alpha-glucosidase inhibitors based on in vitro evidence.

MATERIAL AND METHOD

This research review was conducted based on a literature review. The research flow is presented in Figure 2, using the Google Scholar database with publications from the last ten years written in either Indonesian or English and available in full text. The keywords used in this study to search for relevant literature were “Indonesian plants AND potential inhibitory OR alpha glucosidase AND in vitro.” This systematic review focuses on herbal plant extracts with potential in vitro alpha-glucosidase inhibitory activity. A total of 200 article were screened, 34 articles fulfilled the eligibility criteria.

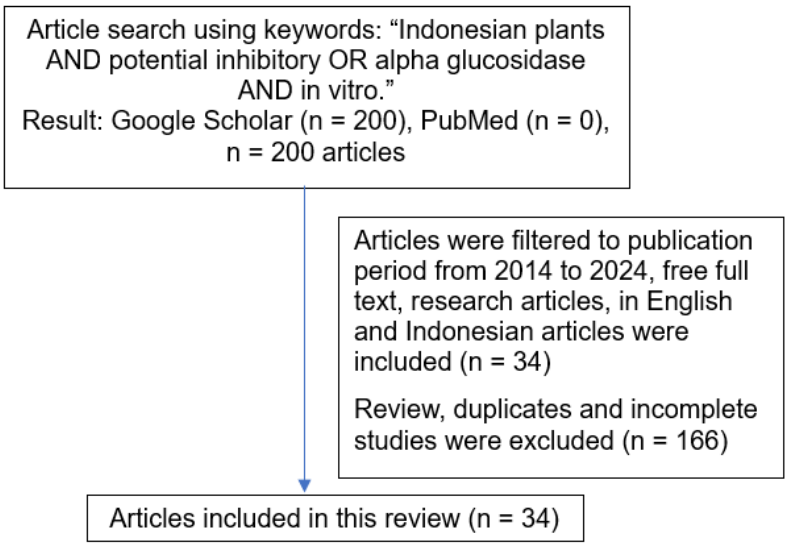


Figure 2. Pathway of Literature Sceening

RESULTS AND DISCUSSION

There are several methods for α-glucosidase inhibition by natural compounds in the newly developed method. The colorimetric-based quantitative method is the most common and practical approach to be used to verify the inhibitory activity of different compounds against the α-glucosidase enzyme. This review mainly discusses the spectrophotometric-based in vitro α-glucosidase inhibitory activity of various plant extracts and their pharmacokinetic properties. The search resulted in 200 articles showing in vitro α-glucosidase inhibition from plants and syntheses that have potential anti-diabetic agents. These articles were then further sorted by in vitro studies. After elimination, 34 articles were specifically tested for in vitro α-glucosidase inhibitory activity. Several previous studies among the 34 articles evaluated in full text in the context of in vitro tests were known to still use conventional extraction methods, one of which was the maceration method to obtain secondary metabolites (Table 1).

Table 1. Plant extracts that have α-glucosidase inhibitory activity

Plant name	Part used	Type of extract	Candidate compound	Mechanism	Method	Ref.
Abelmoschus manihot (L.)	leaves	Ethanol 70% with maceration method	Alkaloids, flavonoids, saponins, steroids and triterpenoids	Involving interactions of active compounds such as flavonoids and terpenoids with the active site of the enzyme, thereby reducing its activity and decreasing the rate of glucose absorption from food	410 nm monitored using a microplate reader	7
Annona muricata	leaves	n-hexane, ethyl acetate, ethanol 96%, and water using maceration method	Muricatin C, cis-Reticulatacin-10-one, and 3-Methylquercetin 7-[galactosyl-(1->4)-glucoside].	Inhibits α-glucosidase through competitive and allosteric binding; active compounds (Muricatin C, cis-Reticulatacin-10-one, 3-Methylquercetin) interact with the enzyme's active site, reducing its catalytic activity and glucose release	The absorbance was measured in a UV-Vis spectrophotometer	8
Ardisia humilis Vahl.	leaves, stems and bark	Methanol 70% using reflux method	Polyphenols or phenolic compounds	The α-glucosidase inhibitory activity is proportional to the total phenolic content Phenolic compounds interact with the enzyme competitively and enhance the antidiabetic effect.	at a wavelength of 413 nm.	9
Artabotrys hexapetalus	breadfruit leaves are yellow and green	Maceration method using ethanol solvent	Hydroxysitansinon IIA in stem extract while phenolic compounds contribute from leaf extract	The mechanism involves competitive inhibition, where terpene (hydroxytanshinone IIA) and phenolic compounds interact with the active site of α-glucosidase, thereby reducing its catalytic activity	measured using at 400 nm using a UV-Vis spectrophotometer	10
Artocarpus altilis	leaves	n-hexane and ethanol 70%, with maceration method	Alkaloids, flavonoids, triterpenoids, steroids, polyphenols	Acts as a competitive inhibitor of α-glucosidase by binding to the enzyme's active site, thereby reducing the hydrolysis of complex carbohydrates into glucose	At 400 nm using a UV-Vis spectrophotometer	11
Aquilaria malaccensis	stems	Soxhlet method using chloroform solvent.	5-Hydroxy-4′,7-dimethoxyflavone and epifriedelanol	Active compounds in *Aquilaria malaccensis*, such as 5-hydroxy-4′,7-dimethoxyflavone and epifriedelanol, inhibit α-glucosidase through hydrogen bonding and hydrophobic interactions. The flavonoid acts competitively, while the triterpenoid contributes via complementary binding	ELISA reader or microplate reader: λ = 405 nm	12

Tinospora crispa (L.)	aerial & wood	Extraction was carried out using maceration method using ethanol 96%.	Terpenoids and terpenoid glycosides	Competitive inhibition through the interaction of active compounds with the enzyme's active site; reduces the catalytic breakdown of disaccharides into glucose	UV–Vis spectrophotometer at 540 nm	13
Caesalpinia sappan, Andrographis paniculata, and *Syzygium cumini*	sawdust	Ethanol 70% is done by maceration method	Homoisoflavanoids, protosappanin, phaeophorbide A methyl ester & saurufuran B	*Caesalpinia sappan*, *Andrographis paniculata*, and *Syzygium cumini* inhibit α-glucosidase through competitive and non-competitive mechanisms. Their bioactive compounds—such as brazilin, andrographolide, quercetin, and other flavonoids—interact with the enzyme's active or allosteric sites, reducing its ability to hydrolyze carbohydrates into glucose	UV-Vis spectrophotometry with λ 400 nm	14
Caesalpinia sappan L. and *Garcinia mangostana*	Rhizomes	70% ethanol-water (1:10) is done by maceration method	Flavanoids	Synergistic inhibition via flavonoid binding at the active site; blocks substrate access and reduces α-glucosidase activity	Absorbance was measured at a wavelength of 405 nm microplate reader	15
Curcuma zanthorrhiza	Rhizomes, leaves, stems, flowers & fruit	Extraction is done by maceration method, the sample is extracted with 75% methanol for 24 hours at room temperature	xanthorrhizol	Competitive inhibition by xanthorrhizol and phenolics binding to the active site; slows oligosaccharide breakdown and postprandial glucose rise.	The absorbance was measured by a microplate reader (Varioskan	16
Etlingera Elatior	bark	Extraction is done by the maceration method, filled with 96% ethanol left for 24 hours	Phenolics, flavonoids, and tannins	Inhibition likely occurs via phenolic and flavonoid compounds interacting with the enzyme's active site, reducing carbohydrate breakdown	Flash, Thermo) at 405 nm.	17
Five Litsea Plants (*Litsea elliptica, Litsea ferruginea, Litsea firma, Litsea garciae,* and *Litsea sp.)*	leaves	The extraction method used is the reflux method with 96% ethanol solvent, with a ratio of 1:10, and extracted for 1 hour	Phenolics and flavonoids	Inhibition of this enzyme by phenolic and flavonoid compounds in *Litsea* species slows carbohydrate digestion, thereby reducing the rapid postprandial entry of glucose into the bloodstream and helping to control blood sugar spikes.	reading of the absorbance at 410 nm with a microplate reader (Epoch Biotech, USA)	18
Piper species (*P. betle*, *P. aduncum*,	leaves	Extracted with methanol using the maceration method	Terpenoids and flavonoids	Terpenoids in *Piper crocatum* (e.g., trans-isoelemicin, myrcene, trans-ocimene) likely inhibit α-glucosidase by reversibly or irreversibly binding to its active site,	Absorbance was measured at a wavelength of 410 nm using a UV-Vis spectrophotometer	19

P. retrofractum, and *P. crocatum*)				preventing substrate interaction and glucose formation		
Garcinia lateriflora	leaves	Simplicity powder is macerated with three different solvents: n-hexane, ethyl acetate, and methanol, for 24 hours	Ethyl acetate extract: Flavonoids, alkaloids, anthraquinone glycosides and tannins	Phenolic compounds such as xanthones and flavonoids in *Garcinia lateriflora* are proposed to inhibit α-glucosidase by binding to its active site, blocking disaccharide hydrolysis and reducing glucose absorption.		20
Gnetum gnemon L.	green tea powder	Extract is macerated with 96% ethanol solvent	Methanol extract: alkaloids, saponins, tannins, glycosides, flavonoids and interquinones	Flavonoids, stilbenes, steroids, and phenolics inhibit α-glucosidase by covalent or non-covalent binding to active site residues, blocking substrate access and carbohydrate hydrolysis	absorbance was recorded at 405 nm using a microplate reader	21
Glochidion arborescens Müll. Arg. Boerl. and *Cynometra ramiflora* (L.)	roots, bark, leaves, and flowers	With maceration method using 96% ethanol	steroids, tannins, polyphenols, flavonoids, and saponins	Phenolic and flavonoid compounds likely inhibit α-glucosidase by competitively binding to its active site, reducing carbohydrate hydrolysis and glucose absorption	activity was carried out using UV-Vis spectrophotometry at a wavelength of 536 nm	22
Camellia sinensis (L.)	Leaves	Conducted by maceration method using 70% methanol	N-hexane extract: steroids/terpenoids	Catechins in green tea, particularly EGCG, inhibit α-glucosidase by binding to active site residues via hydrogen bonds and hydrophobic interactions, or by inducing conformational changes that block substrate access	microplate reader (Versamax ELISA Microplate Reader, USA) was used to measure the absorbance of the solution at 400 nm	23
Gymnanthemum amygdalinum	Leaves	Extracted by maceration using methanol	Luteolin and 3-O-methyl quercetin	Flavonoids like luteolin in *G. amygdalinum* likely inhibit α-glucosidase non-competitively by altering enzyme conformation, reducing carbohydrate metabolism and glucose absorption.	The absorbance of the sample was measured using a microplate reader at 405 nm. The test was carried out in triplicate and was also carried out on a blank (DMSO without sample) and acarbose as a positive control.	24

Hibiscus sabdariffa L	Leaves & stems	Using 70% ethanol solvent by maceration	Flavanoids, polyphenols, tannins and saponins	Flavonoids, anthocyanins, and phenolics in *Hibiscus sabdariffa* inhibit α-glucosidase by binding to its active site and inducing conformational changes, reducing carbohydrate hydrolysis and postprandial glucose levels	ELISA Microplate Reader, was used to measure the absorbance of the solution at 450 nm	25
Melia azedarach L	Leaves	Ethanol	flavonoids such as luteolin, miricetin, and quercetin	Melia azedarach L. extract acts as a partial or competitive inhibitor of α-glucosidase, reducing intestinal glucose absorption and aiding glycemic control	at 410 nm using a microplate reader	26
Merremia peltata L.	Leaves &	hexane, ethyl acetate and methanol using the UAE (Ultrasonic-Assisted Extraction) method	Flavanoids, tannins, polyphenols and saponins	Phenolic and flavonoid compounds in *Merremia peltata* inhibit α-glucosidase competitively by binding to the active site, delaying carbohydrate breakdown and postprandial glucose rise	Microplate Reader (Tecan®), while the control was at 400 nm	27
Moringa oleifera	Fruits	using 13% wet and dry moringa leaf extract	quercetin and kaempferol glycosides, chlorogenic acid, alkaloids, saponins, and triterpenoids	Flavonoids and phenolics in *Moringa oleifera* leaves inhibit α-glucosidase by reversibly or irreversibly binding to its active site, slowing carbohydrate hydrolysis and glucose absorption.	at 400 nm wavelength with microplate reader	28
Lagerstroemia loudonii Teijsm. & Binn	Leaves	extracted using the reflux method with 96% ethanol for one hour.	Flavanoids, catechins and polyphenols	Phenolic compounds in *L. loudonii* competitively inhibit α-glucosidase by binding to its active site, delaying glucose release	Spectrophotometry at 400 nm.	29
Loranthus ferrugineus and *Peperomia pellucida*	Fruit skin, leaves, and seeds	macerated using n-hexane, ethyl acetate, and methanol. The maceration process was carried out 3 times for 24 hours with 30 minutes of ultrasonication.	flavonoids (e.g. quercetin), phenolic complexes, furan derivatives, and phytosterols	Methanol and ethyl acetate extracts of *Loranthus ferrugineus* and *Peperomia pellucida* inhibit α-glucosidase by binding to its active site, blocking carbohydrate hydrolysis and reducing postprandial glucose absorption	absorbance was measured at 405 nm using a microplate reader	30
Parkia speciosa	Fruit skin	Extracted with 3 L of ethanol	Flavanoid compounds, namely Luteolin and 2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3-methoxy-4H-chromen-4-one,	Phenolic and flavonoid compounds in *Parkia speciosa* act as competitive or non-competitive inhibitors of α-glucosidase, reducing carbohydrate hydrolysis and postprandial glucose absorption	Spectrophotometer at a wavelength of 400 nm	31
Pometia pinnata	Stems	96% for 48 hours using the maceration method	phenolics and flavonoids	Phenolics, flavonoids, and tannins in *Pometia pinnata* ethyl acetate extract inhibit α-	colorimetric method at 400.4 nm,	32

				glucosidase by reversibly binding to its active site, reducing disaccharide hydrolysis and postprandial glucose levels.		
Piper crocatum Ruiz & Pav	Leaves	n-Hexane, Ethyl acetate, and Methanol using the maceration method	content in rosella is suggested to play a role in inhibiting	Competitive inhibition via sesquiterpenes and phenolics at α-glucosidase active site	Microplate reader spectrophotometer at 405 nm wavelength.	33
Rhizophora mucronata Lam	Leaves	n-hexane, ethyl acetate, and methanol	the activity of α-amylase and α-/β-glucosidase	Reversible inhibition via flavonoid glycosides at α-glucosidase active site.	Absorbance of sample measured using microplate reader at 405 nm.	34
Sansevieria trifasciata	Seaweed	The *Sansevieria trifasciata* residue was macerated with 13 L of 80% methanol.	phenolic groups,	Flavonoids, alkaloids, and steroids exert competitive and non-competitive inhibition on α-glucosidase, interfering with substrate access and disrupting disaccharide hydrolysis.	UV-Vis spectrophotometer at a wavelength of 400 nm.	35
Sargassum hystrix and *Eucheuma denticulatum*	Powder from species	aquadest, 70% ethanol, and	flavonoids, luteolin, myricetin, and quercetin	Reversible/irreversible binding to active site by polyphenols and phlorotannins	UV-Vis spectrophotometry at 405 nm (Specord 200 Plus by	36
Stenochlaena palustris (Burm.f.)	Seaweed	ethyl acetate	Phytochemical content of phenolics,	Flavonols in *Stenochlaena palustris* bind to the α-glucosidase active site, inhibiting carbohydrate conversion to glucose and supporting glycemic control	UV-Vis spectrophotometer Shimadzu UV-1800	37
Sargassum sp.	Seeds	aquadest, methanol, and chloroform	resin glycosides, and flavonoids	Active site inhibition by phenolics reduces glucose release	monitored at 405 nm, with a Bio Tek Eon microplate reader (Bio Tek, Synergy HT, Vermont, USA)	38
Swietenia mahagoni (L.)	Seeds	Extraction was carried out using methanol three times using the maceration method. Next, the crude methanol extract was partitioned in water (H_2O) and extracted sequentially	Based on the content of antioxidant compounds, amino acids, and various other secondary metabolite compounds.	Alkaloids, triterpenoids, and flavonoids in *Swietenia mahagoni* seeds inhibit α-glucosidase by interfering with carbohydrate breakdown and glucose absorption.	at 410 nm using a microplate ELISA	39

		using n-hexane, dichloromethane, and ethyl acetate.				
Urena lobata	leaves	Extraction was carried out using ethyl acetate	Triterpenoids, ellagic acid,	Stigmasterol, β-sitosterol, and mangiferin from *Urena lobata* inhibit α-glucosidase by forming hydrogen bonds and van der Waals interactions at the active site, reducing enzymatic activity and postprandial glucose absorption.	by measurement of the absorbance utilizing a microplate reader at a wavelength of 405 nm.	40

The inhibitory activity was assessed using UV-Vis spectrophotometry at wavelengths between 400–450 nm, employing p-nitrophenyl-α-D-glucopyranoside (pNPG) as the substrate, which released a yellow compound (p-nitrophenol) upon hydrolysis by the α-glucosidase enzyme. Various plant parts including leaves, stems, roots, rhizomes, and fruits were tested and demonstrated potential as α-glucosidase inhibitors. Secondary metabolites such as flavonoids, alkaloids, tannins, saponins, polyphenols, triterpenoids, and steroids played significant roles in the inhibition mechanisms. Flavonoids, for example, were known to possess hydroxyl groups at positions 3 and 7 that interacted with the enzyme's active site, thereby competitively inhibiting α-glucosidase activity.[41-43]

Extraction plays a critical role in isolating bioactive compounds from medicinal plants, particularly secondary metabolites associated with α-glucosidase inhibitory activity. Conventional methods such as maceration, Soxhlet, and percolation are still widely used due to their simplicity and cost-effectiveness, although they require longer processing times and larger volumes of solvents.[44,45] Among these, maceration remains the most common, as it enables controlled solvent penetration and facilitates the release of metabolites like flavonoids and tannins. However, non-conventional methods such as Ultrasonic-Assisted Extraction (UAE) and Microwave-Assisted Extraction (MAE) offer significant advantages, including reduced solvent use, shorter extraction times, and better preservation of thermolabile compounds.[46] MAE, for instance, utilizes electromagnetic radiation to rupture cell walls and enhance the release of intracellular phytochemicals, making it suitable for extracting sensitive bioactive compounds. Given that many α-glucosidase inhibitors such as polyphenols, flavonoids, and alkaloids are heat- and solvent-sensitive, optimizing the extraction technique is essential to maximize therapeutic potential and support further pharmacological or clinical applications.[47]

Plants containing compounds such as alkaloids, steroids, polyphenols, saponins, tannins, triterpenes, and flavonoids have the potential to inhibit the α-glucosidase enzyme in type 2 diabetes mellitus. Polyphenols in plants are known to inhibit the activity of digestive enzymes through interactions with proteins. The inhibitory activity produced by secondary metabolites, such as polyphenols, steroids, and alkaloids, against carbohydrate-hydrolyzing enzymes can help reduce postprandial hyperglycemia. The inhibitory activity of the α-glucosidase enzyme is related to the content of flavonoids that have hydroxyl groups at positions 3 or 7 so that they can reduce inhibitory activity.[18] Alkaloid compounds help regenerate pancreatic β cells so that they can lower blood glucose and increase insulin secretion through extra-pancreatic mechanisms. Covering the mechanisms in increasing glycogen synthesis, improving glucose transport in the intestine, and inhibiting glucose synthesis by inhibiting the enzymes glucose-6-phosphatase and fructose-1,6-bisphosphatase in the gluconeogenesis process is important. The inhibition process can reduce the formation of glucose from non-carbohydrate sources and promote glucose oxidation through glucose-6-phosphate dehydrogenase.[48] Flavonoids are phenolic compounds that have a low molecular weight composed of 2-phenylchromone, including acetic acid derivatives. Flavonoids are 15-carbon polyphenol compounds composed of 2 benzene rings linked to 3 linear chains.[2] Flavonoids have the potential to overcome diabetes mellitus, including glucose regulation, increasing insulin secretion and sensitivity, glucose utilization in peripheral tissues, and inhibiting glucose absorption in the intestine.[48,49]

CONCLUSION

Based on our findings, in vitro studies on Indonesian medicinal plants demonstrated α-glucosidase inhibitory activity. Indonesian Plants have bioactive

compounds such as flavonoids, polyphenols, alkaloids, tannins, and saponins. These compounds act primarily through competitive inhibition by slowing carbohydrate hydrolysis and reducing postprandial glucose levels. These results support the potential use of Indonesian herbal plants as natural α-glucosidase inhibitors and reinforce their relevance in the development of alternative antidiabetic therapies with fewer side effects.

AUTHORS' CONTRIBUTIONS

Joanne Natalie Leiwakabessy: Data curation, Methodology, Writing- Original draft preparation. Marisca Evalina Gondokesumo: Conceptualization, Writing- Reviewing and Editing. Mariana Wahjudi: Visualization, Writing- Reviewing and Editing,

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