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Antidiabetic medicinal plants of Indonesia: their in silico, in vitro, in vivo and clinical trial studies

Ari Satia Nugraha · Kintoko Kintoko · Chintya Permata Zahky Sukrisno Putri · Fatima Az-Zahra · Lilla Nur Firli · Dinar Mutia Rani · Yoshinta Debby Purnomo · Phuong Thuy Viet Nguyen · Rara Merinda Puspitasari · Tri Hartati · Bawon Triatmoko · Antonious Nugraha Widhi Pratama · Dinar Sari Cahyaningrum Wahyuni · Handa Muliasari · Paul Anthony Keller · Phurpa Wangchuk

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Abstract The tropical islands of Indonesia house the second largest biodiversity in the world. For generations, indigenous communities have relied on medicinal plants to treat various ailments, including diabetes. However, no comprehensive systematic review has been conducted to consolidate research progress in this area. This review aims to investigate and summarize the current research landscape on antidiabetic medicinal plants in Indonesia. Data collection, collation and analysis were performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Relevant publications on the antidiabetic evaluation of Indonesian medicinal plants were retrieved from leading scientific databases, including **Scifinder®** and **Garuda**, yielding a total of 108 eligible articles. Several notable compound screening studies identified bioactive phytochemicals with significant antidiabetic potential, such as quinine as a SIRT1 activator, prunetin as an aldose reductase inhibitor, gallic acid as a pancreatic α-amylase (PPA) inhibitor, oleanolic acid as a PTP1B inhibitor, and 3,4,5-tri-*O*-caffeoylquinic acid methyl ester as an α-glucosidase inhibitor. Additionally, clinical investigations and community-based trials reported significant blood glucose-lowering effects from botanical extracts including *Piper crocatum*, *Moringa oleifera*, and *Curcuma xanthorrhiza* in diabetic patients. Recognizing the therapeutic potential of indigenous botanicals, the Indonesian government has intensified its support for the development of scientifically standardized herbal medicines aimed at diabetes treatment, positioning them as part of the country's integrated healthcare system.

A. S. Nugraha (✉) · C. P. Z. S. Putri · F. Az-Zahra · L. N. Firli · D. M. Rani · Y. D. Purnomo · B. Triatmoko · A. N. W. Pratama
Drug Utilisation and Discovery Research Group, Faculty of Pharmacy, Universitas Jember, Jember, Indonesia 68121
e-mail: arisatia@unej.ac.id

C. P. Z. S. Putri
e-mail: chintyapermata97@gmail.com

F. Az-Zahra
e-mail: fatimahbdw8@gmail.com

L. N. Firli
e-mail: lillanurfirli13@gmail.com

D. M. Rani
e-mail: dinarmutiarani@gmail.com

Y. D. Purnomo
e-mail: yoshinta05@gmail.com

B. Triatmoko
e-mail: bawon.farmasi@unej.ac.id

A. N. W. Pratama
e-mail: anton.farmasi@unej.ac.id

A. S. Nugraha · P. A. Keller
School of Science, University of Wollongong, Wollongong, NSW 2522, Australia
e-mail: keller@uow.edu.au

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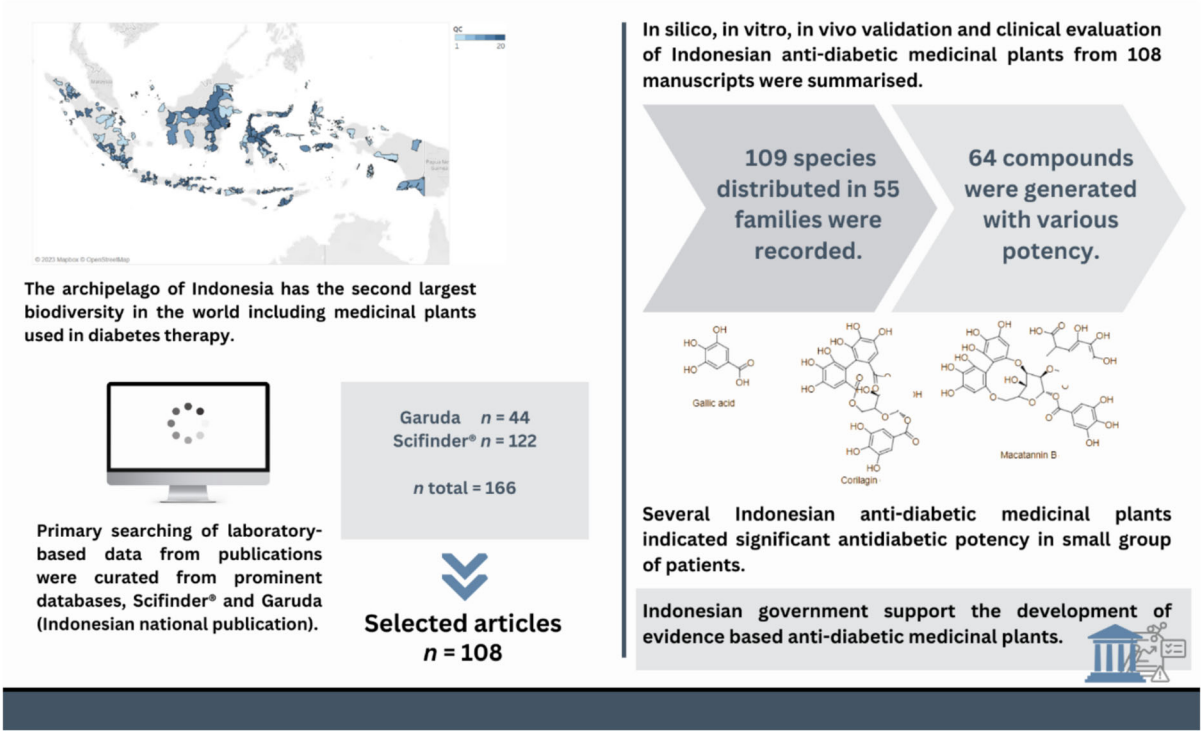
Graphical abstract



Keywords Antidiabetic · Indonesian medicinal plants · In silico · In vitro, in vivo · Clinical · Indonesian herbal medicine · Phytopharmaceuticals

K. Kintoko
Faculty of Pharmacy, Ahmad Dahlan University, Umbulharjo, Yogyakarta 55164, Indonesia
e-mail: kintoko@pharm.uad.ac.id

P. T. V. Nguyen
Faculty of Pharmacy, University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh City 700000, Vietnam
e-mail: ntvphuong@ump.edu.vn

R. M. Puspitasari
Faculty of Pharmacy and Health Sciences, Royal College of Medicine Perak, Universiti Kuala Lumpur, 30450 Ipoh, Perak, Malaysia
e-mail: raramerinda@unikl.edu.my

T. Hartati
PT Bintang Toedjoe, Kawasan Greenland International Industrial Centre (GIIC) BB No.7, Desa Sukamahi–Central Cikarang, Bekasi, West Java 17530, Indonesia
e-mail: marcello.chien@gmail.com

D. S. C. Wahyuni
Pharmacy Department, Faculty of Mathematics and Sciences, Universitas Sebelas Maret, Surakarta, Indonesia
e-mail: dinarsari_cw@mipa.uns.ac.id

H. Muliasari · P. Wangchuk (✉)
College of Science and Engineering, James Cook University, Cairns Campus, Smithfield, QLD 4878, Australia
e-mail: phurpa.wangchuk@jcu.edu.au

H. Muliasari
e-mail: handa.muliasari@my.jcu.edu.au

P. Wangchuk
Australian Institute of Tropical Health and Medicine, James Cook University, Cairns Campus, Smithfield, QLD 4878, Australia

Introduction

Diabetes is a chronic disease characterized by either the pancreas' inability to produce sufficient insulin or the body's inability to effectively utilize the insulin it produces. There are three main types of diabetes: Type 1 diabetes (T1D), Type 2 diabetes (T2D), and Gestational diabetes (GD) (WHO 2023). While T1D is not preventable, the onset of T2D and GD can often be delayed or prevented through appropriate lifestyle modifications. Poor dietary habits, physical inactivity, and other aspects of an unhealthy lifestyle contribute to metabolic dysfunction, which can lead to degenerative diseases such as diabetes and its hallmark symptom, hyperglycemia (Ratnadewi et al. 2020). According to the International Diabetes Federation (IDF), in 2021, the global prevalence of diabetes was estimated at 537 million people aged 20–79 years, with annual healthcare costs reaching 1 trillion US dollars (IDF 2021). Alarmingly, this figure is projected to rise to 637 million within the next two decades (IDF 2021). Within Southeast Asia, the prevalence of diabetes ranks third globally, and Indonesia ranks fifth in the world, with approximately 19.5 million cases (IDF 2021). This data highlights diabetes as a critical public health concern, affecting not only adults but an increasing number of younger individuals, with the prevalence in Indonesia increasing annually (IDF 2021) (O'Rourke et al. 2020). Beyond its health implications, diabetes imposes substantial socioeconomic burdens, diminishing national productivity and quality of life while significantly increasing healthcare expenditures. The worldwide diabetes epidemic is primarily driven by T2D, which is characterized by impaired insulin action and/or abnormal insulin secretion (American Diabetes Association 2020). The initial metabolic abnormality typically involves insulin resistance in key tissues such as muscle, liver, and adipose tissue, resulting in a reduced cellular response to insulin. Alternatively, the defect may manifest at a systemic level, where the blood glucose-lowering effect of both endogenous and exogenous insulin is diminished (Taylor 2012; Roberts et al. 2013). In addition to insulin, several pharmacological classes of glucose-lowering agents are in the management of diabetes, including insulin sensitizers and secretagogues (such as sulfonylureas and meglitinides), thiazolidinediones, α-glucosidase inhibitors, and newer drug modalities such as incretin-based therapies (DPP-4 inhibitors and GLP-1 receptor agonists), amylin analogues, SGLT-2 inhibitors, bile acid sequestrants, dopamine-2 agonists (Roberts et al. 2013; Meneses et al. 2015; Association 2020). Commonly prescribed drugs such as metformin, sulfonylureas and semaglutide (Ozempic®), which is also approved for weight loss, are frequently utilized in T2D management. However, these treatments are often associated with adverse effects, including transient edema, inflammation, and fat hypertrophy, and gastrointestinal disturbances (Roberts et al. 2013). Moreover, there remains no definitive cure for T1D. An alternative therapeutic approach involves targeting carbohydrate hydrolyzing enzymes, particularly α-amylase, which plays a crucial role in the breakdown of polysaccharides into simpler sugars (Tamarai et al. 2019). The synthetic α-amylase inhibitor **acarbose** has become a standard antidiabetic agent within this class. Despite its efficacy in reducing postprandial hyperglycemia, acarbose is associated with notable gastrointestinal side effects, including flatulence, diarrhea, abdominal bloating, discomfort, and, in rare cases, hepatitis (Cantley and Ashcroft 2015).

Empirical-based herbal treatments for diabetes have been widely practiced in many countries and are often associated with low toxicity and minimal side effects (Ratnadewi et al. 2020; Nisar et al. 2017). As an archipelagic nation with the second largest biodiversity in the world, Indonesia possesses a rich repository of medicinal plants used for managing diabetes. Home to over 300 ethnic groups, Indonesia's diverse cultural heritage includes a wealth of, and rich herbal medicine traditions passed down through generations. A significant initiative, the RISTOJA survey project, spearheaded by the Ministry of Health of the Republic of Indonesia, successfully curated 2,256 medicinal plant species through consecutive programs conducted in 2012, 2015 and 2017 (B2P2TOOT 2012; 2015; 2017). Among these, 250 species were specifically recorded as being traditionally used for diabetes therapy across various regions of the country (Fig. 1). In recent years, Indonesian pharmaceutical companies have increasingly turned to traditional knowledge as a foundation for antidiabetic drug discovery (Tjokroprawiro et al. 2016). For example, studies on *Lagerstroemia speciosa* and *Cinnamomum burmannii* revealed that their bioactive extracts can ameliorate insulin resistance by restoring insulin receptor phosphorylation (Tjokroprawiro et al.

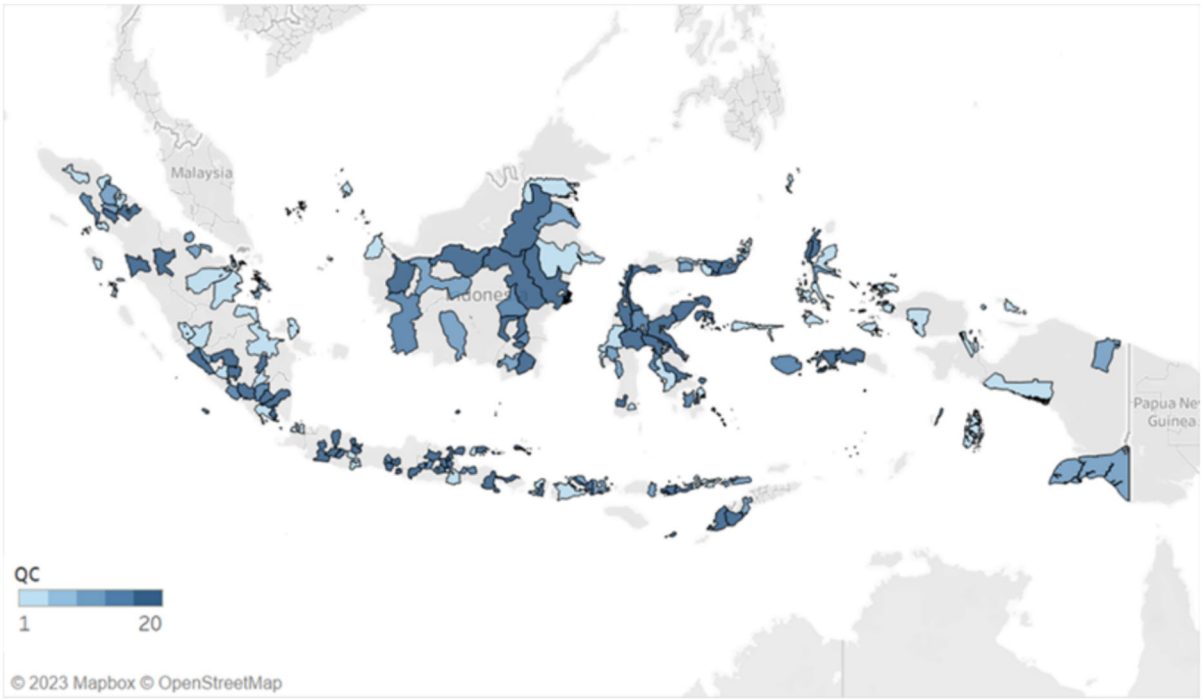


Fig. 1 Map of Indonesia illustrating the distribution density of reported medicinal plants traditionally used for diabetes therapy and management by indigenous communities across the archipelago. Darker blue regions indicate a higher prevalence of herbal medicines use for diabetes treatment

2016). These extracts were also found to enhance GLUT-4 (glucose transporter) translocation from the cytoplasm to the membrane, upregulate PPAR γ, thereby resulting new GLUT-4 synthesis, and suppress TNF-α induced by lipolysis—mechanisms crucial for improving glucose homeostasis (Tjokroprawiro et al. 2016). In addition, research on bitter melon fruit (*Momordica charantia*) showed that its nonpolar extract fractions can significantly stimulate insulin secretion from pancreatic beta cells, highlighting its therapeutic potential as a natural antidiabetic agent (Shimada et al. 2022).

Despite these promising studies, no comprehensive review has yet been published on the bioprospecting of Indonesian medicinal plants for antidiabetic applications. In this review, a systematic and literature-based approach was undertaken involving data curation, collation, analysis and discussion to provide new insights into ethnopharmacological practices of antidiabetic therapy across the Indonesian archipelago. An intensive literature mining was conducted using two major databases, Scifinder® (www.scifinder-n.cas.org) and Garuda (www.garuda.kemdikbud.go.id), the national database of scholarly publications managed by the Ministry of Education, Culture, Research and Technology of the Republic of Indonesia. Standard English keywords included Indonesia AND medicinal plants or Herbs AND diabetes or hyperglycemia. Indonesian search terms such as herbal or *tanaman obat* or *Jamu* AND diabetes or *kencing manis* or *hiperglikemik*. Additionally, specific keywords related to computational studies, enzyme-based evaluation, in vitro and in vivo antidiabetic evaluation and clinical validation of Indonesian medicinal plants were incorporated into the search strategy. Through this systematic literature mining process, a total of 166 articles published between 1990 and 2023 were initially retrieved (Fig. 2). Studies lacking essential information, particularly incomplete data on plant identity or therapeutic use were excluded. Ultimately, 108 articles containing full-text data met the inclusion criteria and formed the basis for data curation, analysis, and the findings discussed in this review.

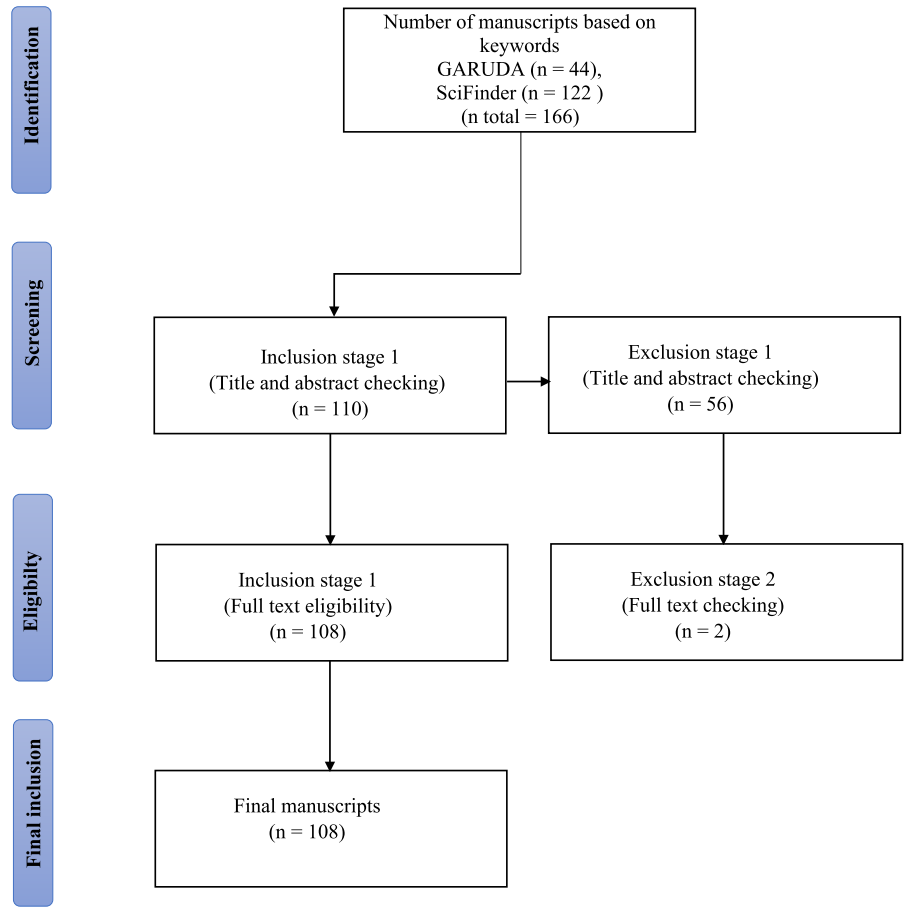


Fig. 2 Flow diagram of the systematic literature search and selection process for studies on Indonesian antidiabetic medicinal plants, conducted using Scifinder® and Garuda databases

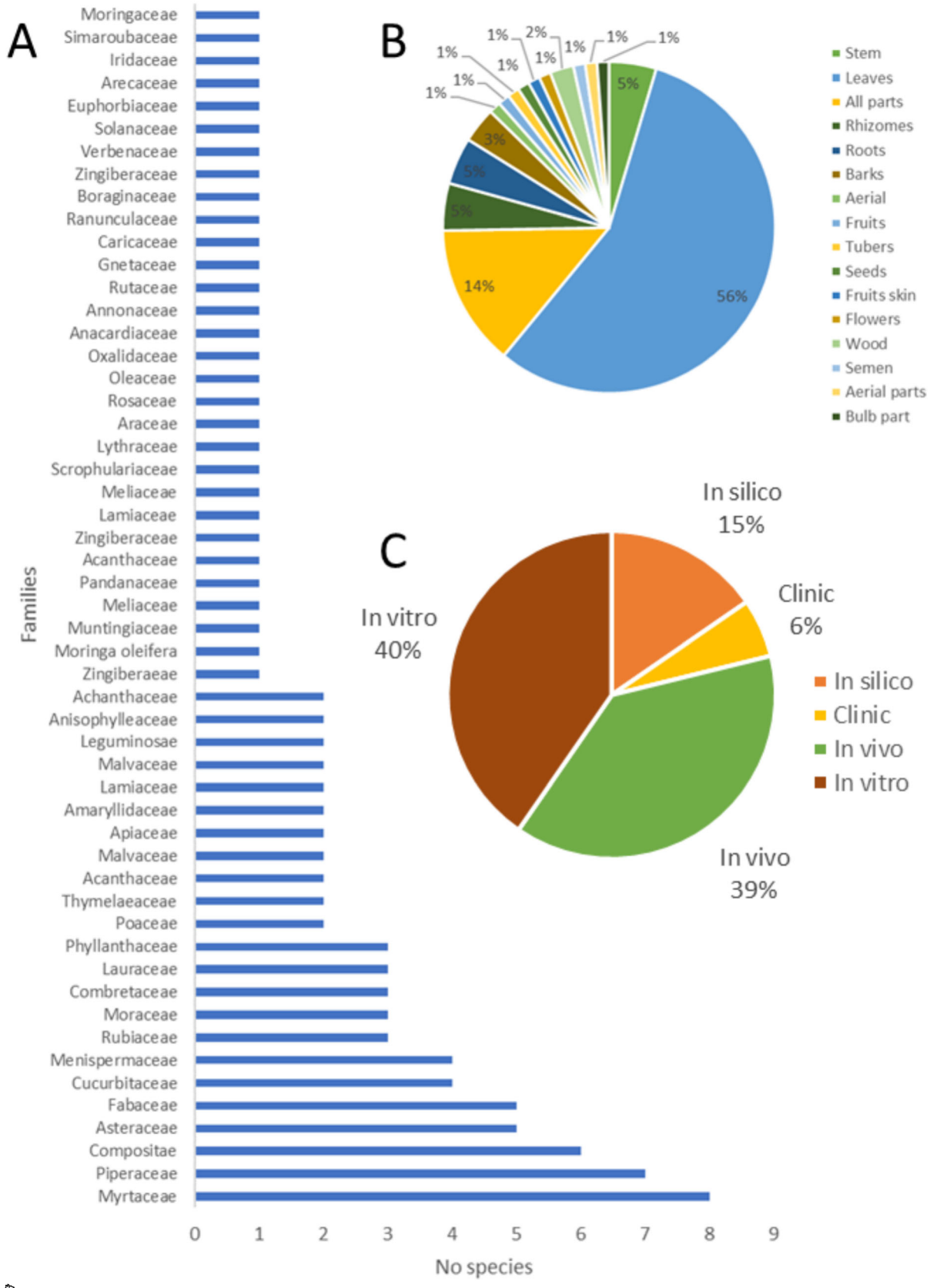
Plant families, mode of uses and scientific studies reported by 108 articles

A meta-analysis of 108 full-text articles, covering 109 species of medicinal plants, revealed that these species belonged to a total of 55 families (Fig. 3A). Among them, the Myrtaceae ranked first with 8 species reported for use in diabetes treatment in Indonesia. This was followed by Piperaceae (7 species), Compositae (6 species), and both Asteraceae and Fabaceae (5 species each). The Mornigaceae family, along with 29 other families, ranked lowest with only 1 species each reported for use in treating diabetes. When analyzing the plant parts used in treatment, leaves were the most commonly utilized, accounting for 56%, followed by the use of whole parts (14%), and stems, aerial parts and fruits, each contributing 5% (Fig. 3B).

The included publications were also assessed based on the type of scientific investigation conducted (Fig. 3C). Of the 108 articles, 40% were based on in vitro assessments, followed closely by in vivo animal studies (39%). In silico computer modeling approaches accounted for 15% of the studies. Additionally, clinical trials made up 6% of the research on medicinal plants used in Indonesia for diabetes treatment.

In silico studies of Indonesian antidiabetic medicinal plants

Computational chemistry has facilitated the virtual screening of interactions between ligands or drug leads and target enzymes. This approach offers a significant advantage by drastically reducing screening time compared to conventional in vitro bioassay guided protocols. Moreover, advancements in Artificial intelligence-assisted phytochemical techniques and modern instrumentation have streamlined the


A
Moringaceae
Simaroubaceae
Iridaceae
Arecaceae
Euphorbiaceae
Solanaceae
Verbenaceae
Zingiberaceae
Boraginaceae
Ranunculaceae
Caricaceae
Gnetaceae
Rutaceae
Annonaceae
Anacardiaceae
Oxalidaceae
Oleaceae
Rosaceae
Araceae
Lythraceae
Scrophulariaceae
Meliaceae
Lamiaceae
Zingiberaceae
Acanthaceae
Pandanaceae
Meliaceae
Muntingiaceae
Moringa oleifera
Zingiberaeae
Achanthaceae
Anisophylleaceae
Leguminosae
Malvaceae
Lamiaceae
Amaryllidaceae
Apiaceae
Malvaceae
Acanthaceae
Thymelaeaceae
Poaceae
Phyllanthaceae
Lauraceae
Combretaceae
Moraceae
Rubiaceae
Menispermaceae
Cucurbitaceae
Fabaceae
Asteraceae
Compositae
Piperaceae
Myrtaceae
Families
0 1 2 3 4 5 6 7 8 9
No species
B
56%
14%
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5%
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2%
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1%
1%
1%
Stem
Leaves
All parts
Rhizomes
Roots
Barks
Aerial
Fruits
Tubers
Seeds
Fruits skin
Flowers
Wood
Semen
Aerial parts
Bulb part
C
In silico 15%
Clinic 6%
In vivo 39%
In vitro 40%
In silico
Clinic
In vivo
In vitro

◀**Fig. 3** Meta analysis of 108 articles covering 109 plant species. A. Species distribution of antidiabetic plants by family. B. Plant parts used and studied for treating diabetes. C. Type of studies involved in antidiabetic studies of Indonesian medicinal plants

isolation and characterisation of secondary metabolites, accelerating the discovery of bioactive molecules from natural products. The increasing availability of secondary metabolite databases from medicinal plants has further enabled targeted computation-based drug screening. Several studies have successfully complemented these in silico findings with in vitro validation. The 108 articles featured these advancements and screening techniques, as discussed below. In particular, several Indonesian medicinal plants traditionally used for diabetic treatment have been investigated through metabolomics profiling to identify their bioactive constituents. One such study analysed the leaves of *Smallanthus sonchifolius* (Poepp) H. Robinson collected from Lembang, West Java, Indonesia. Metabolomics analysis identified 28 compounds, which were subsequently evaluated for their α-glucosidase inhibitory activity using molecular docking. The study revealed that several compounds (Fig. 4), nystose **1**, 1-kestose **2**, luteolin-3′-7-di-*O*-glucoside **3**, and 1,3-*O*-dicaffeoilquinic acid **4** isomers exhibited docking score from − 100.216 to − 115.657 kcal.mol^{-1}. These values were comparable to that of the standard drug acarbose **5**, which had a docking score of − 115.774 kcal/mol (Aziz et al. 2021).

Studies on the crude ethyl acetate extract from the fruits of *Terminalia catappa* L. demonstrated inhibitory activity against α-glucosidase with an IC_{50} value of 192.51 µg/mL, compared to the positive control, acarbose, which had an IC_{50} of 17.52 µg/mL. Phytochemical profiling of the crude extracts using GC–MS led to the identification of thirteen compounds. Further analysis of the GC–MS data, combined with in silico approach to identify active phytoconstituents (Fig. 5) revealed *β*-sitosterol **6**, *β*-sitosterol acetate **7** and sitostenone **8** as potential antidiabetic agents, with binding energy values of − 10.61, − 11.14, and − 9.79 kcal/mol, respectively (Sari et al. 2016).

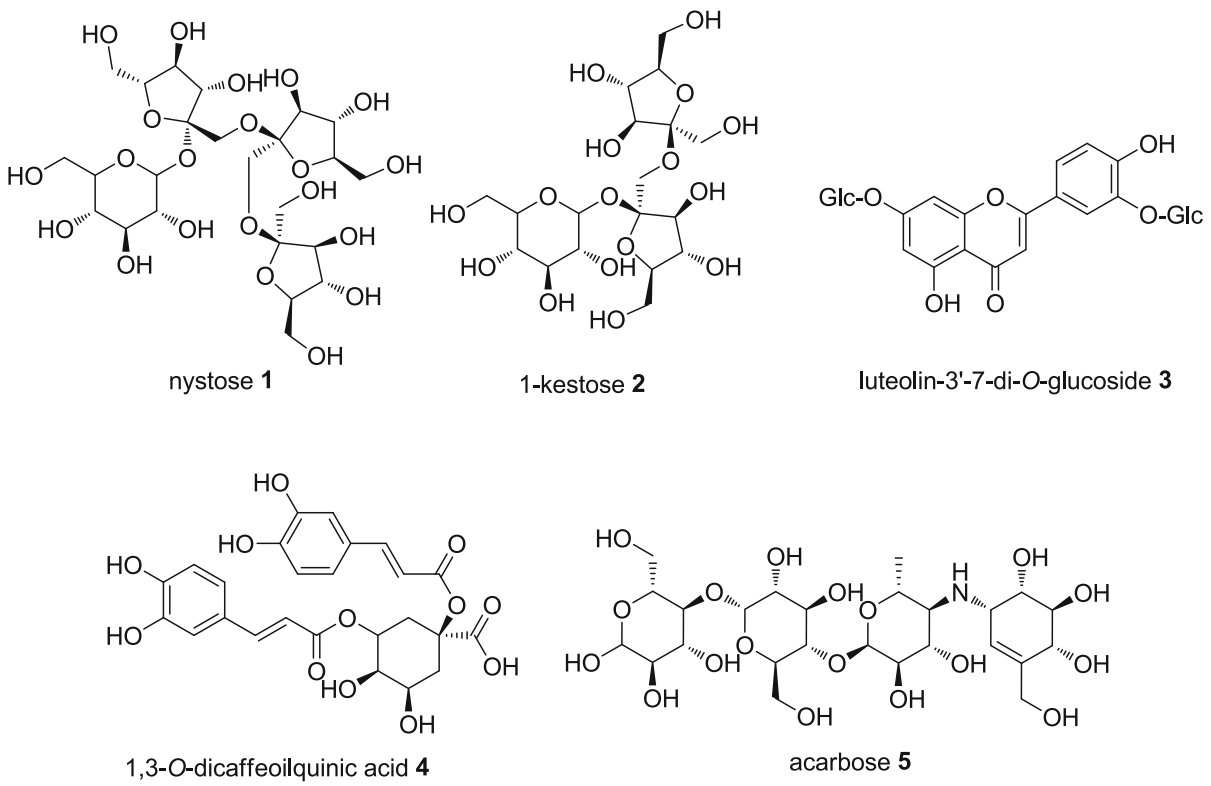


Fig. 4 Antidiabetic compounds **1**–**4** from *Smallanthus sonchifolius* and the standard drug acarbose **5**

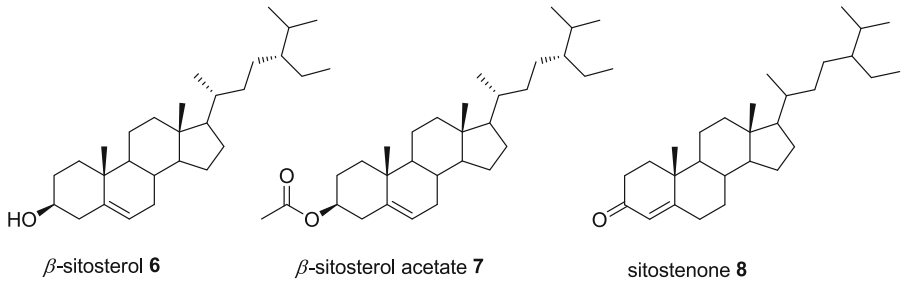


Fig. 5 Antidiabetic compounds **6–8** from *Terminalia catappa*

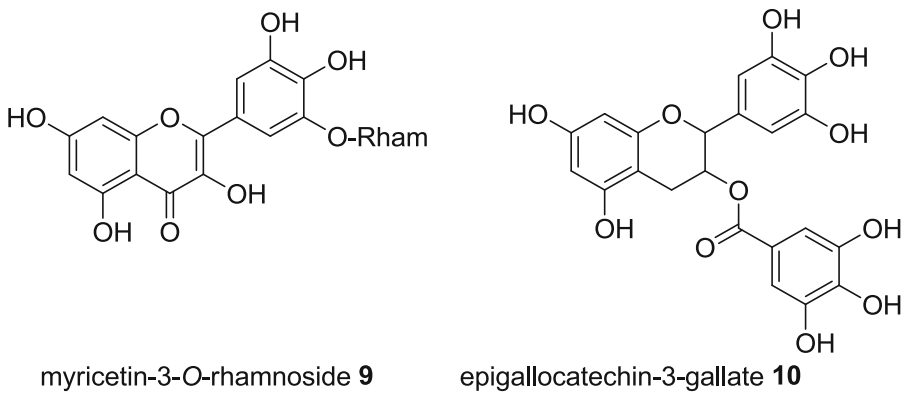


Fig. 6 Antidiabetic compounds **9–10** isolated from *Syzygium polyanthum*

A decoction of the leaves of *Syzygium polyanthum* (Wight) Walp (Myrtaceae) is traditionally prepared by Indigenous communities in Indonesia to help lower blood glucose levels. Metabolomics investigations on leaf samples collected from Bogor, Indonesia, identified fractions responsible for α-glucosidase inhibitory activity. Further spectrometric and spectroscopic analyses of these fractions revealed the presence of myricetin-3-*O*-rhamnoside **9** and epigallocatechin-3-gallate **10** (Fig. 6). Docking experiments showed that both compounds exhibited strong binding affinities to the α-glucosidase active site, with binding energy values of -8.47 and -8.19 kcal/mol, respectively, compared to the positive control acarbose **5,** which had a binding energy value of -10.13 kcal/mol (Syabana et al. 2022).

GC–MS based phytochemical profiling of *Psychotria malayana* Jack leaves obtained from Jambi, Indonesia, successfully identified nine metabolites. Their antidiabetic potential was evaluated through molecular docking experiments targeting α-glucosidase. Among the identified compounds, cholesta-7,9(11)-diene-3-ol **11**, β-tocopherol **12** and stigmast-5-ene **13** exhibited notable binding affinities, with energy values of − 6.1, − 8.6, − 9.4 kcal/mol, respectively. These results were comparable to those of quercetin **14** and the control ligand ADG, which showed binding energies of − 8.4 and − 6.0 kcal/-mol, respectively (Fig. 7) (Nipun et al. 2021).

Some species of Indonesian medicinal plants used to treat diabetes are also found in other countries. Therefore, in addition to conducting in-house phytochemical studies on samples collected in Indonesia, it is beneficial to document and compare metabolites from the same species collected elsewhere. However, due to differences in habitat and ecological conditions, the chemical composition and biological activities of these plants may vary significantly. While data from other countries can offer valuable scientific insights, it is advisable to study Indonesian medicinal plants locally whenever financial resources permit. For instance, a study of *Imperata cylindrica* (L.) P. Beauv. Collected in Indonesia identified 5-methoxyflavone **15**, 6-hydroxy-5-methoxyflavone **16**, 7-hydroxy-4-methoxy-5-methylcoumarin **17**, and siderin **18** as potential α-glucosidase inhibitors, demonstrating binding activities comparable to the standard miglitol (Fig. 8) (Rohman et al. 2021). Similarly. in silico investigations of constituents from *Solanum torvum* Sw. (Takokak plant) suggested methyl caffeate **19** as a

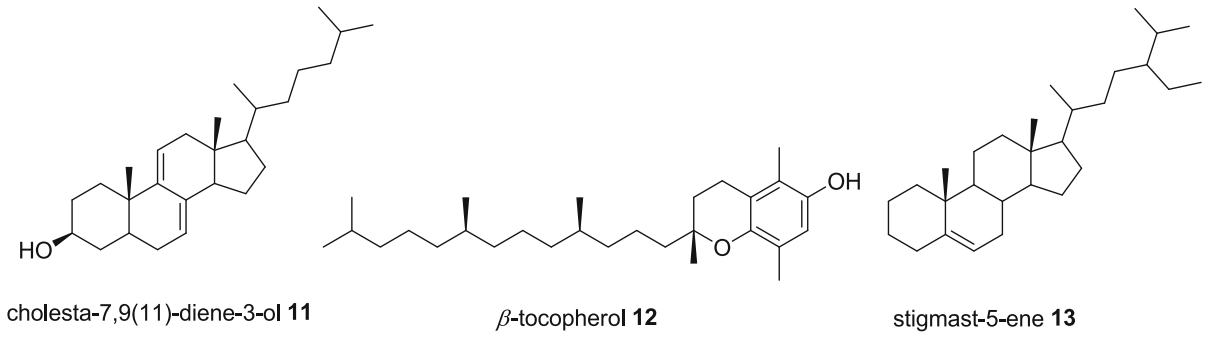
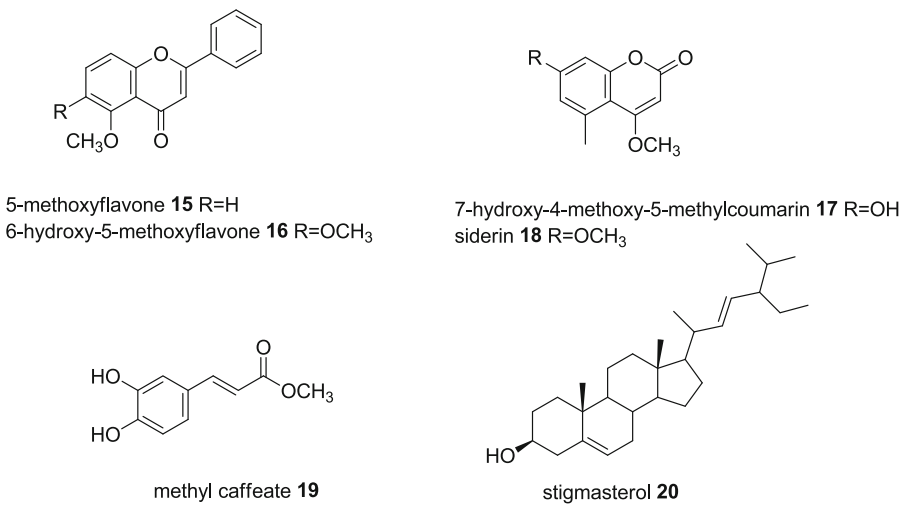


Fig. 7 Antidiabetic compounds **11**–**13** derived from *Psychotria malayana*

Fig. 8 Antidiabetic compounds derived from *Imperata cylindrica, Solanum torvum* and *Morinda citrifolia*



potential antidiabetic marker, with a binding affinity of -6.8 kcal.mol^{-1} against α-glucosidase (Fig. 8)(Putri et al. 2022).

Phytosterol constituents of *Morinda citrifolia* L., specifically stigmasterol **20** and *β*-sitosterol **6** were also evaluated in silico for their antidiabetic potential. Docking studies were conducted using multiple targets: α-amylase (2QV4), α-glucosidase (5NN8), PPAR-*γ* (2P4Y), and DPP-IV (4PNZ) (Fig. 8). The results showed that both sterols exhibited stronger binding affinities with α-amylase than the standard ligan/drug acarbose **5** (Lolok et al. 2022).

Another important protein target in antidiabetic research is dipeptidyl peptodase-IV (DPP-IV), which plays a role in increasing incretin levels, thereby contributing to the reduction of blood glucose levels. Secondary metabolites extracted from the fruit, leaves and stems of *Momordica charantia* L. have been reported to exhibit DPP-IV inhibitory activity, which charantin **21** identified as the most potent, showing a binding energy of -9.8 kcal/mol surpassing that of the native ligand PF2, which had a binding energy of -8.7 kcal/mol (Deviana and Diniatik 2021). Similarly, phytochemicals from *S. sonchifolius*, including 13(*R*)-hydroxyoctadeca-(9*E*,11*E*,15*Z*)-trienoic acid **22**, benzylalcohol 7-*O*-α-L-arabinopyranosyl(1“ → 2’)-*β*-D-glucopyranoside **23**, 13(*R*)-hydroxyoctadeca-(9*Z*,11*E*,15*Z*)-trienoic acid **24,** were evaluated for DPP-IV inhibitory activity. However, none of these compounds demonstrated a higher binding affinity than the standard inhibitor, sitagliptin (Fig. 9) (Sinurat et al. 2021). The same docking protocol was applied to Ongga (*Strychnos lucida* R.Br.), where ten previously reported phytoconstituents were screened against several antidiabetic targets, including human aldose reductase (2HV5), human maltase-glucoamylase (2QMJ), PPAR-gamma (3TY0), pancreatic beta-cell SUR1 (6PZA), and human DPP-IV (3BJM). While

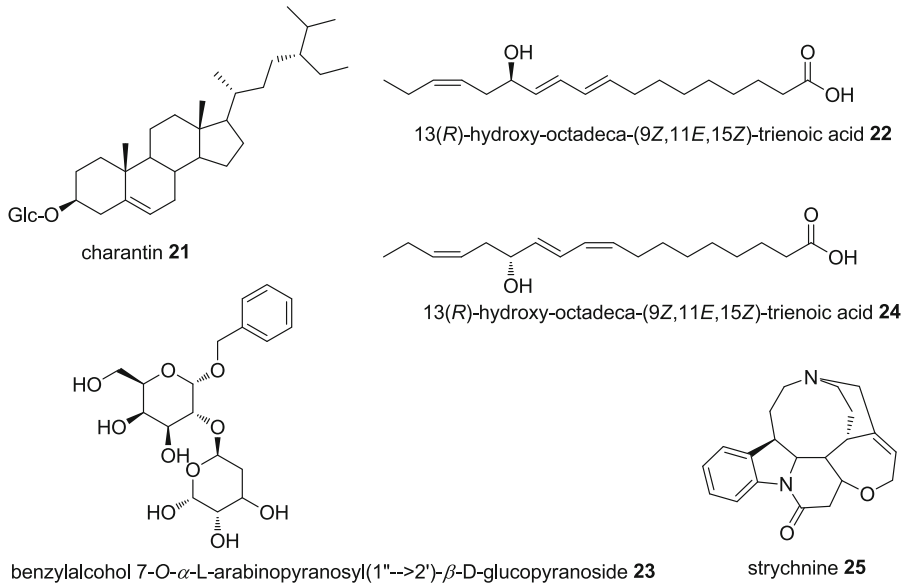


Fig. 9 Antidiabetic compounds originated from *Momordica charantia* and *Strychnos lucida*

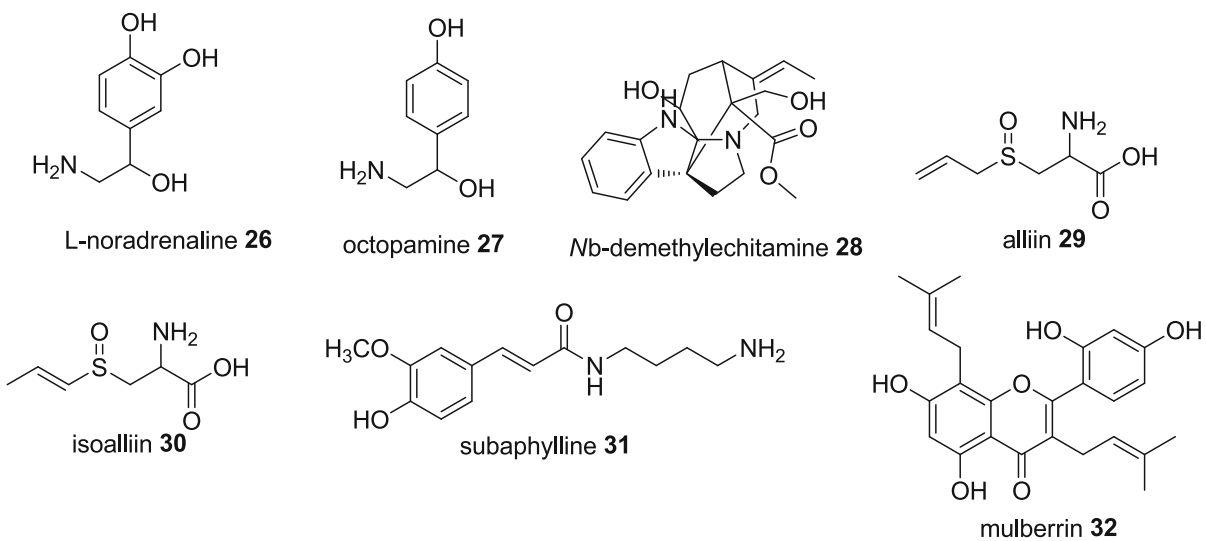


Fig. 10 Antidiabetic compounds identified through structure-based screening of secondary metabolites from the Indonesian Herbal Database

most compounds exhibited lower binding affinities compared to their respective native ligands, strychnine **25** showed notable DPP-IV inhibitory potential with a binding energy of -6.2 kcal/mol, outperforming the standard drug vildagliptin (− 5.4 kcal/mol) (Fig. 9) (Setiawansyah et al. 2022).

Studies utilizing the extensive Indonesian medicinal plants database (Indonesian Herbal Database)—which comprises 1,377 compounds- identified six potential DPP-IV inhibitory agents: L-noradrenaline **26**, octopamine **27**, *N*b-demethylechitamine **28**, alliin **29**, isoalliin **30**, and subaphylline **31** (Farkhani et al. 2020; Naeem et al. 2012). In addition, a structure-based pharmacophore virtual screening conducted using compounds from the same database highlighted mulberrin **32** as the most promising candidate for

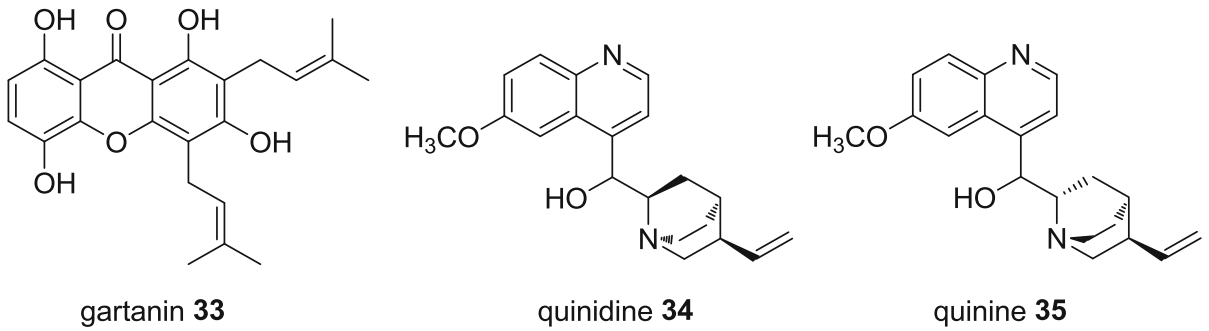


Fig. 11 Secondary metabolites from Indonesian medicinal plants as potential SIRT1 activator candidates

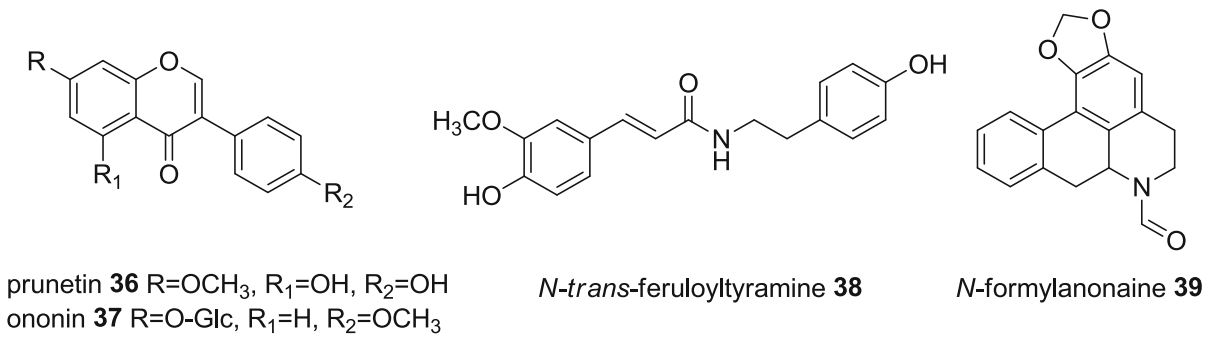


Fig. 12 Phenolic and alkaloid antidiabetic compounds generated through ligand-based in silico virtual screening of secondary metabolites from Indonesian medicinal plants database

SIRT1 activator. This prediction was subsequently validated through an in vitro bioassay, which confirmed its activity with an IC_{50} value of 2.10 µM (Fig. 10) (Azminah et al. 2019).

In silico ligand-based screening using the Indonesian medicinal plant database, which comprises 1,377 compounds, identified gartanin **33**, quinidine **34**, and quinine **35** as the top candidates for SIRT1 activation (Fig. 11). Furthermore, in vitro experiments confirmed the SIRT1-activating potential of these compounds, demonstrating IC_{50} values of 2.10, 1.79, 1.71, 1.14 µM, respectively (Azminah et al. 2019).

Compounds from the Indonesian medicinal plant database was also screened for their potential as aldose reductase inhibitors using Random Forest (RF) modelling. This analysis suggested two compounds, prunetin **36** and ononin **37**, as having the highest RF scores. Subsequent in vitro experiments indicated inhibitory activities of 58% and 52%, respectively, at a concentration of 15 µM (Fig. 12) (Naeem et al. 2012).

Beyond molecular docking approaches, computational studies also utilized molecular similarity assessments with approved drug molecules, i.e. employing the Tanimoto molecular index. One such study evaluated 595 compounds from four commonly used medicinal plants, pare (*Momordica charantia* L.), sembung (*Blumea balsamifera* (L.) DC.), bratawali (*Tinospora crispa* (L.) Hook. f. & Thomson), and jahe (*Zingiber officinale* Roscoe). The results revealed that *T. crispa derived compounds, N-trans*-feruloyltyramine **38** and *N*-formylanonaine **39,** exhibited the highest similarity index when compared with 19 FDA-approved antidiabetic agents (Fig. 12) (Bakri et al. 2016).

In vitro studies of Indonesian antidiabetic medicinal plants

To date, several in vitro studies have investigated various Indonesian medicinal plants for their potential anti-hyperglycaemic properties (Table 1). These studies have evaluated 57 plant species from 32 different families, focusing on phytochemicals extracted from

Table 1 In vitro antidiabetic activity of Indonesian medicinal plants

Family	Species	Part	Sample	Object/target	IC_{50}	Inhibition percentage	Positive control	Ref.
Acanthaceae	*Andrographis paniculata* (Burm.f.) Wall. ex Nees	Herb	Ethanol extract	DPP-IV		37.03 ± 0.65%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)
	Ruellia tuberosa L	Leaves	Ethanol extract	DPP-IV		30.09 ± 1.30%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)
Anisophyllaceae	*Anisophyllea disticha* Baill	Leaves	Triterpene isolate 1	α-glucosidase	46.246 ± 0.166 μg/mL		Acarbose = 19.737 ± 0.046 μg/mL	Fikriyah et al. (2020)
			Triterpene isolate 2		80.273 ± 0.080 μg/mL			
		Leaves	Methanol extract	α-glucosidase	47.765 ± 0.127 μg/mL		Acarbose = 18.283 ± 0.375 μg/mL	Almurdani et al. (2020)
Apiaceae	*Centella asiatica* (L.) Urb	Leaves	Methanol extract	α-amylase		42.3 ± 4.7%		Gunawan-Puteri et al. (2012)
Apocynaceae	*Catharanthus roseus* (L.) G.Don	Bark	Methanol extract	α-amylase		45.3 ± 2.8%		Gunawan-Puteri et al. (2012)
	Parameria barbata K.Schum	Bark	Methanol extract	α-amylase		17.4 ± 2.8%		Gunawan-Puteri et al. 2012)
Arecaceae	*Areca cathecu* Burm.f	Fruit	Methanol extract	α-amylase		92.5 ± 7.9%		(Gunawan-Puteri et al. (2012)
Asteraceae	*Artemisia vulgaris* L	Leaves	Methanol extract	α-amylase		84.3 ± 2.8%		Gunawan-Puteri et al. (2012)
	Chromolaena odorata (L.) R.M.King & H.Rob	Leaves	Ethyl acetate extract	α-glucosidase	779.54 ± 6.16 μg/mL		Acarbose = 7.67 ± 1.86 μg/mL	Putri and Fatmawati (2019)
			Odoratenin		> 62.5 μg/mL			
			Isosakuranetin		> 312.5 μg/mL			
	Gynura procumbens (Lour.) Merr	Stalk and leaves	Methanol extract	α-amylase		28.2 ± 8.5%		Gunawan-Puteri et al. (2012)
	Pluchea indica (L.) Less	Leaves	3,5-di-*O*-caffeoylquinic acid	α-glucosidase	1166 μM		Acarbose = 0.5 μM	Arsiningtyas et al. (2014)
			4,5-di-*O*-caffeoylquinic acid methyl ester		208 μM			
			3,4,5-tri-*O*-caffeoylquinic acid methyl ester		2 μM			

Table 1 continued

Family	Species	Part	Sample	Object/target	IC_{50}	Inhibition percentage	Positive control	Ref.
			3,4,5-tri-*O*-caffeoylquinic acid		13 µM			
			1,3,4,5-tetra-*O*-caffeoylquinic acid		11 µM			
	Cosmos caudatus Kunth	Leaves	Ethanol extract	α-glucosidase	77.17 ± 37.08 µg/mL		Quercetin = 1.38 ± 0.433 µg/mL	Firdaus et al. (2021)
	Smallanthus sonchifolius (Poepp.) H.Rob	Leaves	Ethanol extract	DPP-IV		52.84 ± 2.01%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)
	Tithonia diversifolia (Hemsl.) A.Gray	Leaves	Ethanol extract	DPP-IV		16.8 ± 1.34%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)
	Wedelia biflora (L.) DC	Leaves	Methanol extract	α-glucosidase	211.15 µg/mL			Mangallo et al. (2019)
			Chloroform extract		112.56 µg/mL			
Boraginaceae	*Cordia myxa* L	Leaves	Ethanol extract	α-glucosidase	35.89 µg/mL		Acarbose = 117.20 µg/mL	Malik and Ahmad (2016)
Combretaceae	*Terminalia catappa* L	Fruit	Ethyl acetate extract	α-glucosidase	192.51 µg/mL		Acarbose = 17.52 µg/mL	Sari et al. (2016)
Convolvulaceae	*Merremia mammosa* (Lour.) Hallier f	Rhizome	Ethanol extract	DPP-IV		17.12 ± 1.95%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)
		Leaves	*n*-hexane extract	α-glucosidase		66.19 ± 0.41%	Acarbose = 54.85 ± 1.48%	Ratnadewi et al. (2020)
Costaceae	*Costus speciosus* (J.Koenig) Sm	Leaves	Ethanol extract	DPP-IV		25.92 ± 21.60%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)
Cucurbitaceae	*Momordica charantia* Descourt	Semen	Ethanol extract	DPP-IV		41.66 ± 1.63%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)
Cymodoceaceae Vines	*Cymodocea rotundata* Asch. & Schweinf	All parts	Ethanol extract	α-glucosidase	429.28 ± 8.89 µg/mL		Acarbose = 197 ± 3.07 µg/mL	Widiyanto et al. (2018)
Euphorbiaceae	*Antidesma bunius* (L.) Spreng	Leaves	Ethyl acetate extract	α-amylase α-glucosidase	α-amylase: 95.39 ± 4.27%α-glucosidase: 93.17 ± 4.95%		Acarboseα-amylase: 91.06 ± 2.15%α-glucosidase: 54.85 ± 1.48%	Ratnadewi et al. (2020)
	Antidesma montanum Blume	Leaves	Ethyl acetate extract, n-hexane extract	α-amylase α-glucosidase	α-amylase: 46.45 ± 4.03%α-glucosidase: 79.84 ± 3.46%		Acarboseα-amylase: 91.06 ± 2.15%α-glucosidase: 54.85 ± 1.48%	Ratnadewi et al. (2020)
	Euphorbia cotinifolia L	Leaves	Ethanol extract	DPP-IV		23.61 ± 3.27%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)

Table 1 continued

Family	Species	Part	Sample	Object/target	IC_{50}	Inhibition percentage	Positive control	Ref.
	Euphorbia hirta L	Herb	Ethanol extract	DPP-IV		33.52 ± 0%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)
	Macaranga tanarius Müll.Arg	Leaves	Methanol extract	α-amylase		18.6 ± 1.4%		Gunawan-Puteri et al. (2012)
	Phyllantus urinaria L	Stalk and leaves	Aqueous methanol extract	α-amylase		98.0 ± 5.8%		Gunawan-Puteri et al. (2012)
			Gallic acid			23%		
			Corilagin			21%		
			Macatannin B			33%		
Fabaceae	*Abrus precatorius* L	Leaves	Lupenone	Porcine pancreatic α-amylase	31 μM			Yonemoto et al. (2014)
			Luteolin		3.1 mM			
			Extract		71%			
	Pterocarpus indicus Willd	Leaves	Ethanol extract	DPP-IV		25.0 ± 27.16%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)
Hydrocharitaceae	*Enhalus acoroides* (L.f.) Royle	All parts	Ethanol extract	α-glucosidase	168.15 ± 2.71 μg/mL		Acarbose = 197 ± 3.07 μg/mL	Widiyanto et al. (2018)
	Thalassia hemprichii (Ehrenb.) Asch	All parts	Ethanol extract	α-glucosidase	425.86 ± 5.15 μg/mL		Acarbose = 197 ± 3.07 μg/mL	Widiyanto et al. (2018)
Lauraceae	*Cinnamomum cassia* (L.) D.Don	Fruits	Methanol extract	α-amylase		50.4 ± 2.4%		Gunawan-Puteri et al. (2012)
	Cinnamomum burmanii (Nees &T.Nees) Blume	Bark	Aqueous extract	α-glucosidase		20%		Nurdin and Sukohar (2017)
	Persea americana Mill	Semen	Ethanol extract	DPP-IV		6.48 ± 0.32%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)
Leguminosae	*Trigonella foenum* graecum L	Semen	Ethanol extract	DPP-IV		71.29 ± 0.33%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)
Lhytraceae	*Lagerstroemia speciosa* (L.) Pers	Leaves	Methanol extract	α-amylase α-glucosidase	α-amylase: 90.82 ± 2.70% α-glucosidase: 94.44 ± 0.43%		Acarbose α-amylase: 91.06 ± 2.15% α-glucosidase: 54.85 ± 1.48%	Ratnadewi et al. (2020)
	Lagerstroemia loudonii Teijsm. & Binn	Leaves	Ethanol extract	DPP-IV		60.22 ± 2.01%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)

Table 1 continued

Family	Species	Part	Sample	Object/target	IC_{50}	Inhibition percentage	Positive control	Ref.
	Punica granatum L	Rind	Ethanol extract	DPP-IV		58.79 ± 2.23%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)
		Fruit peels	Methanol extract	α-amylase		35.4 ± 0.8%		Gunawan-Puteri et al. (2012)
Meliaceae	*Azadirachta indica* A. Juss	Leaves	Ethanol extract	DPP-IV		17.78 ± 1.02%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)
			Methanol extract	α-amylase		3.5 ± 2.8%		Gunawan-Puteri et al. (2012)
	Swietenia mahagoni (L.) Jacq	Semen	Ethanol extract	DPP-IV		38.88 ± 22.25%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)
Menispermaceae	*Arcangelisia flava* (L.) Merr	Leaves	Ethyl acetate extract, methanol extract	α-amylase α-glucosidase	α-amylase: 64.24 ± 3.53% α-glucosidase: 95.04 ± 3.55%		Acarbose α-amylase: 91.06 ± 2.15% α-glucosidase: 54.85 ± 1.48%	Ratnadewi et al. (2020)
	Tinospora crispa Miers	Stem	Ethanol extract	DPP-IV		65.86 ± 1.02%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)
		Bark	Methanol extract	α-amylase		16.1 ± 0.3%		Gunawan-Puteri et al. (2012)
Moraceae	*Artocarpus heterophyllus* Lam	Leaves	Ethanol extract	DPP-IV		30.55 ± 4.90%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)
	Ficus religiosa L	Leaves	Ethanol extract	DPP-IV		68.98 ± 1.95%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)
Myrtaceae	*Syzygium aromaticum* (L.) Merr. & L.M.Perry	Flower	Methanol extract	α-amylase		16.1 ± 0.3%		Gunawan-Puteri et al. (2012)
	Syzygium polyanthum (Wight) Walp	Leaves	Ethanol extract	*p*-nitrophenyl-α-D-glucopyranoside		97.37%		Dewijanti et al. (2019)
		Leaves	Acetone water fraction	α-glucosidase	24.8 μg/mL	97.34%	Acarbose = 0.38 μg/ml	Syabana et al. (2022)
Piperaceae	*Piper betle* L	Leaves	Ethanol extract	α-amylase		71.9% in 5 mg/mL concentration		Chauhan et al. (2020)
	Piper crocatum Ruiz & Pav	Leaves	Ethanol extract	α-glucosidase		1.29%—40.80%	Acarbose = 80.97%	Muhammad et al. (2020)
Plantaginaceae	*Plantago major* L	Roots	Methanol extract	α-amylase		67.6 ± 6.6%		Gunawan-Puteri et al. (2012)

Table 1 continued

Family	Species	Part	Sample	Object/target	IC_{50}	Inhibition percentage	Positive control	Ref.
Rutaceae	*Lunasia amara* Blanco	Leaves	Methanol extract	α-amylase α-glucosidase	α-amylase: 90.49 ± 2.95% α-glucosidase: 83.33 ± 3.20%		Acarbose α-amylase: 91.06 ± 2.15% α-glucosidase: 54.85 ± 1.48%	Ratnadewi et al. (2020)
Simaroubaceae	*Brucea javanica* (L.) Merr	Fruits	Methanol extract	α-amylase		7.3 ± 0.39%		Gunawan-Puteri et al. (2012)
Solanaceae	*Physalis angulata* L	Leaves	Ethanol extract	DPP-IV		13.94 ± 4.08%	Sitagliptin = 74.77 ± 0.3%	Riyanti et al. (2016)
Thymelaeaceae	*Phaleria macrocarpa* Boerl	Fruit peels	Ethanol extract	α-glucosidase	1.60 ± 0.04 mg/L		Acarbose = 1.33 ± 0.03 mg/L	Irawan et al. (2022)
Verbenaceae	*Lantana camara* L	Aerial parts	24-Hydroxylantadene B	Protein tyrosine phosphatase 1B (PTP1B)	7.3 μM		Oleanolic acid = 1.3 μM	Abdjul et al. (2017)
			24-Hydroxylantadene D		> 18 μM			
			24-Hydroxylantadene X		> 18 μM			
			22-Hydroxy-4-epi-hederagonic acid		> 21 μM			
			3β-Hydroxylantadene C		7.3 μM			
			Icterogenin		11 μM			
			4-*epi*-Hederagonic acid		8.1 μM			
			Oleanolic acid		2 μM			
			22β-Oleanolic acid		7.9 μM			
			3β-Hydroxylantadene A		7.2 μM			
			3β-Hydroxy		5.1 μM			
			lantadene B		6.9 μM			
			22-Hydroxyoleanonic acid		5.5 μM			
			Lantadene B		5.2 μM			
			Lantadene A		6.9 μM			
			Oleanonic acid		7.9 μM			
			Lantadene D		10.5 μM			
			Pomonic acid		10.6 μM			
			Pomolic acid		7.5 μM			
			Lantanilic acid		5.1 μM			

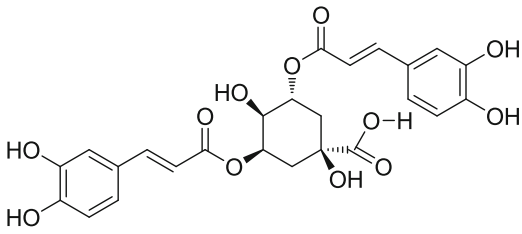
Table 1 continued

Family	Species	Part	Sample	Object/target	IC_{50}	Inhibition percentage	Positive control	Ref.
			Camaric acid		> 16 µM			
			Pectolinarin		> 33 µM			
			Lantanolic acid		7.3 µM			
			22*β*-Tigloyloxylantanolic acid		> 16 µM			
			Hispidulin		> 33 µM			
			Pectolinarigenin			36% inhibition at 32 µM		
	Zingiberaceae	*Curcuma longa* L	Rhizome	Aqueous extract	α-glucosidase		Single extract = 2.930 mg/dL	
		Zingiber officinale Roscoe	Rhizome	Aqueous extract	α-glucosidase		< 25%	

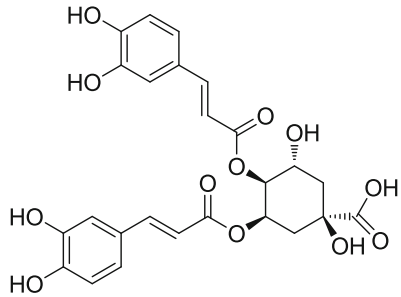
leaves, fruits, seeds, barks, fruit peels, aerial parts, rhizomes, roots, stalks, and flowers. Most samples were prepared as crude extracts, and antidiabetic activity was assessed using enzymatic assays targeting α-glucosidase, α-amylase, dipeptidyl peptidase-IV (DPP-IV), *p*-nitrophenyl-α-D-glucopyranoside, protein tyrosine, phosphatase 1B, and porcine pancreatic α-amylase. The results of these in vitro experiments were reported as IC_{50} values and/or percentage inhibition. Among the tested species, those belonging to eleven plant families, including Asteraceae, Boraginaceae, Convolvulaceae, Euphorbiaceae, Hydrocharitaceae, Lythraceae, Menispermaceae, Myrtaceae, Rutaceae, Thymelaeaceae, and Verbenaceae demonstrated varying degrees of antidiabetic activity.

Asteraceae

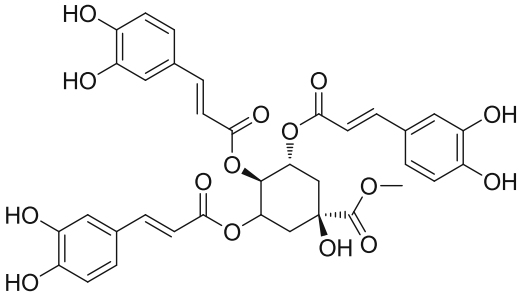
The in vitro evaluation of the Asteraceae family focused on several species, including *Smallanthus sonchifolius* (Poepp.) H.Rob., *Tithonia diversifolia* (Hemsl.) A.Gray., *Artemisia vulgaris* L., and *Gynura procumbens* (Lour.) Merr, *Chromolaena orodara* (L.) R.M. King & H. Rob, and *Wedelia biflora* (L.) DC. These species exhibited moderate to low activity against glucose metabolism-related enzymes, with IC_{50} values ranging from 62.5 to 779.5 µg/mL and inhibition percentages ranging from 16.8 ± 1.34 to 84.3 ± 2.8% (Gunawan-Puteri et al. 2012; Mangallo et al. 2019; Putri and Fatmawati 2019; Riyanti et al. 2016). A phytochemical investigation of *Pluchea indica* (L.) Less. led to the isolation several caffeoylquinic acid derivatives: 3,5-di-*O*-caffeoylquinic acid **40**, 4,5-di-*O*-caffeoylquinic acid methyl ester **41**, 3,4,5-tri-*O*-caffeoylquinic acid methyl ester **42**, 3,4,5-tri-*O*-caffeoylquinic acid **43**, and 1,3,4,5-tetra-*O*-caffeoylquinic acid **44** (Fig. 13)(Arsiningtyas et al. 2014). Interestingly, compounds **42**, **43** and **44** demonstrated strong α-glucosidase inhibitory activity, with IC_{50} values of 2, 11 and 13 µM, respectively, compared to acarbose as the positive control (IC_{50} = 0.5 µM). In contrast, compounds **40** and **41** were significantly less active, with IC_{50} values of 208 and 1166 µM, respectively (Arsiningtyas et al. 2014). Previous studies discovered that the methyl esterification of the quinic acid moiety enhance α-glucosidase inhibitory activity, and the number of caffeoyl groups contributes significantly to the compound's



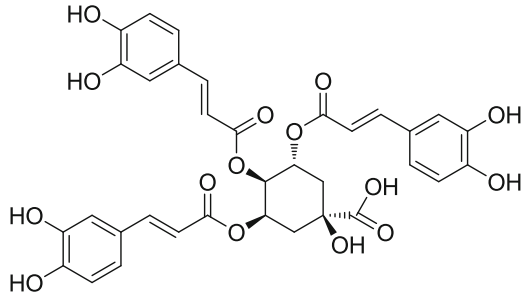
3,5-di-*O*-caffeoylquinic acid **40**



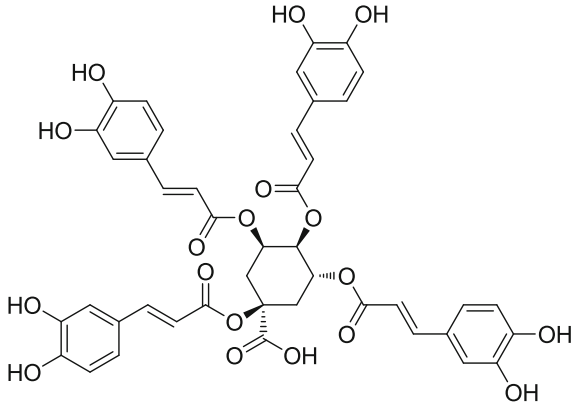
4,5-di-*O*-caffeoylquinic acid methyl ester **41**



3,4,5-tri-*O*-caffeoylquinic acid methyl ester **42**



3,4,5-tri-*O*-caffeoylquinic acid **43**



1,3,4,5-tetra-*O*-caffeoylquinic acid **44**

Fig. 13 Caffeoylquinic acid derivatives from Indonesian *Pluchea indica* with antidiabetic potential

enzyme inhibition potential (Arsiningtyas et al. 2014). Therefore, caffeoylquinic acid derivatives from *P. indica* may hold promise as therapeutic agents for the management of postprandial hyperglycaemia.

Boraginaceae

An in vitro study on the Boraginaceae species, *Cordia myxa* L. showed that its ethanol extract exhibited higher α-glucosidase inhibitory activity than the positive control, acarbose with IC_{50} values of 35.89 and 117.20 µg/mL, respectively (Malik and Ahmad 2016).

Convolvulaceae

The medicinal plant *Merremia mammosa* (Lour.) Hallier f., which belongs to the Convolvulaceae family, has been reported to possess antidiabetic properties (Ratnadewi et al. 2020). The *n*-hexane extract obtained from *M. mammosa* leaves demonstrated moderate inhibitory activity, reaching up to

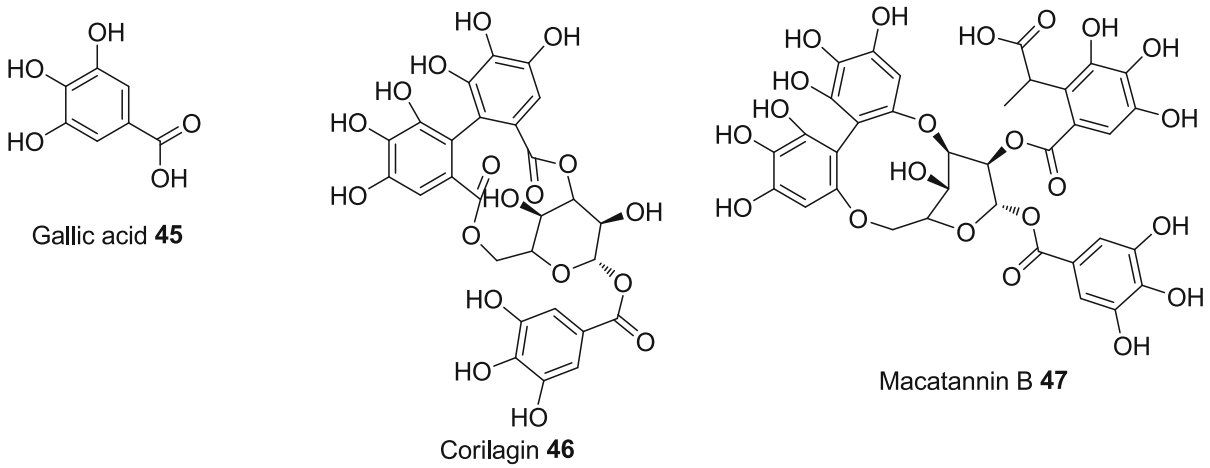


Fig. 14 Gallic acids derivatives with antidiabetic activities from *Phyllantus urinaria* herbs

66.19 ± 0.41% at a concertation of 25 µgGAE/mL. Notably, the inhibitory effect was considerably significant compared to the positive control, acarbose, which showed 54.85 ± 1.48% inhibition (Ratnadewi et al. 2020).

Euphorbiaceae

A study conducted on *Euphorbia cotinifolia* L. and *Euphorbia hirta* L., both belonging to the Euphorbiaceae family, demonstrated weak α-glucosidase inhibitory activity, with respective inhibition values of 23.61 ± 3.27 and 33.52 ± 0%. These result was considerably lower compared to the standard positive control drug, sitagliptin, which exhibited 74.77 ± 0.3% inhibition at a concentration of 2.5 µg/mL (Riyanti et al. 2016). Similarly, the crude extract of *Macaranga tanarius* Müll.Arg. failed to significantly impede the DPP-IV enzyme, showing an inhibition level of 18.6 ± 1.4% at a concentration of 5 mg/mL (Gunawan-Puteri et al. 2012). In contrast, the ethyl acetate extract of *Antidesma bunius* (L.) Spreng. leaves demonstrated strong hypoglycemic activity, with α-glucosidase and α-amylase inhibition values of 93.17 ± 4.95 and 95.39 ± 4.27%, respectively, at a concentration of 25 µgGAE/mL (Ratnadewi et al. 2020). A significant decrement in α-glucosidase activity was also reported in an in vitro study on *Antidesma montanum* Blume., where the *n*-hexane leaf extract showed 79.84 ± 3.46% inhibition at the same concentration (Ratnadewi et al. 2020). These findings indicate that at concentration of 25 µgGAE/mL, *A. bunius* and *A. montanum* extracts exhibit more pronounced enzyme inhibitory effects compared to acarbose, which showed 54.85 ± 1.48% inhibition against α-glucosidase and 91.06 ± 2.15% against α-amylase (Ratnadewi et al. 2020). Furthermore, previous investigations revealed the antidiabetic potential of the aqueous methanol extract of *Phyllantus urinaria* L. against porcine pancreatic amylase (PPA), along with three isolated compounds namely gallic acid **45**, corilagin **46**, and macatannin B **47** (Fig. 14) (Gunawan-Puteri et al. 2012). These compounds showed PPA inhibitory activity values of 98.0, 23, 21, and 33%, respectively, at a concentration of 5 mg/mL. However, despite their promising antidiabetic activity, the absence of a standard positive control drug limits the ability to fully assess and compare their effectiveness.

Hydrocharitaceae

Among the species in the Hydrocharitaceae family, *Enhalus acoroides* (L.f.) Royle. was examined for its antidiabetic potential and demonstrated α-glucosidase inhibitory activity with an IC_{50} value of 168.15 ± 2.71 µg/mL. The ethanolic extract of *E. acoroides* showed significant activity comparable to that of the positive control, acarbose (IC_{50} = 197 ± 3.07 µg/mL) (Widiyanto et al. 2018). In comparison, the α-glucosidase inhibition assay of *Thalassia hemprichii* (Ehrenb.) Asch. ethanol extract displayed weaker activity, with an IC_{50} value of

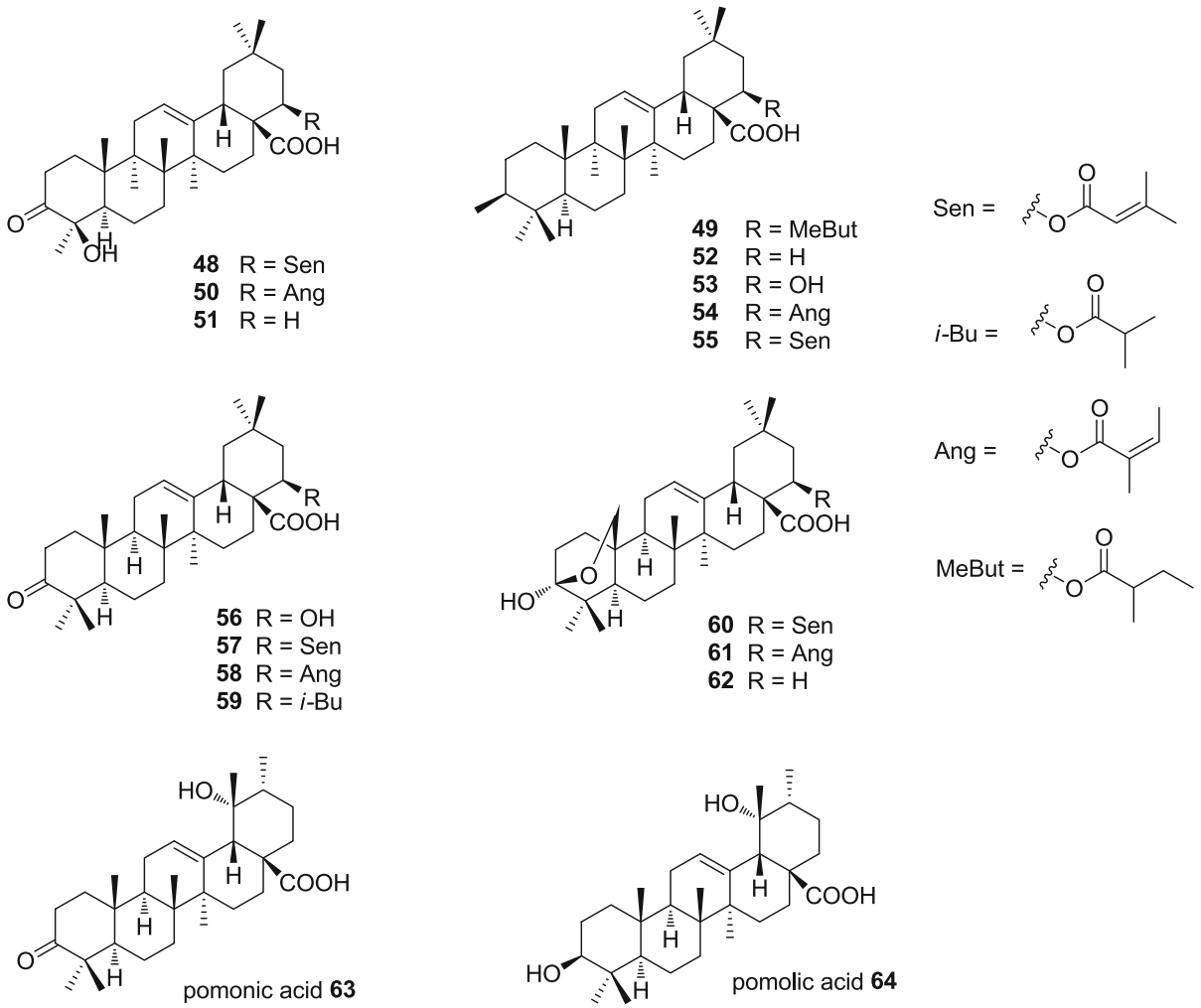


Fig. 15 Bioactive compounds from medicinal plants of the Verbenaceae family with the potential to modulate carbohydrate metabolism

425.86 ± 5.15 µg/mL compared to acarbose (IC_{50} = 197 ± 3.07 µg/mL) (Widiyanto et al. 2018).

Lhytraceae

From the three species in the Lhytraceae family, only the methanol extract of *Lagerstroemia speciosa* (L.) Pers. leaves showed notable α-glucosidase inhibition, achieving 83.33 ± 3.20%, surpassing that of the positive control, acarbose (54.85 ± 1.48%) (Ratnadewi et al. 2020). Contrarily, crude extracts of *Lagerstroemia loudonii* Teijsm. & Binn., and *Punica granatum* L. displayed lower DPP-IV inhibitory activity than the standard drug sitagliptin (74.77 ± 0.3%), with values of 60.22 ± 2.01 and 58.79 ± 2.23%, respectively (Riyanti et al. 2016).

Menispermaceae

Tinospora crispa Miers., a member of Menispermaceae family, has been traditionally use in diabetic treatment. However, in vitro evaluation of its 96% ethanolic stem extract revealed only modest DPP-IV inhibitory activity (65.86 ± 1.02%)at a concentration of 2.5 µg/mL, which was lower than that of sitagliptin (74.77 ± 0.3%) (Riyanti et al. 2016). Conversely, bioassay-guided screening of *Arcangelisia flava* (L.) Merr., a well-known medicinal plant, revealed strong α-glucosidase inhibitory activity. Its methanol leaf

extract displayed 94.44 ± 0.43% inhibition at 25 µgGAE/mL, comparable to acarbose (54.85 ± 1.48%) (Ratnadewi et al. 2020). Nevertheless, no further phytochemical studies were performed to isolate its bioactive constituents.

Myrtaceae

Prior investigations have reported the antidiabetic activity of two Indonesian medicinal plants from the Myrtaceae family, namely *Syzygium polyanthum* (Wight) Walp. and *Syzygium aromaticum* (L.) Merr. & L.M.Perry. The ethanol extract of *S. polyanthum* leaves exhibited strong enzymatic hydrolysis inhibition of *p*-nitrophenyl-α-D-glucopyranoside (97.37%), though no standard control was used (Dewijanti et al. 2019). In another study of the acetone water extract from the same species showed α-glucosidase inhibitory activity with an IC_{50} of 24.8 µg/mL, which was subordinate to its positive control, acarbose (IC_{50} = 0.38 µg/mL) (Syabana et al. 2022). *S. aromaticum,* commonly known as '*cengkeh'*, is a tropical evergreen plant with typical aromatic flower buds. The methanol flower extract exhibited poor α-amylase inhibition (35.4 ± 0.8%) at a concentration of 5 mg/mL (Gunawan-Puteri et al. 2012).

Rutaceae,

Lunasia amara Blanco, a sparsely branched shrub and the only investigated Indonesian species in the Rutaceae family, has shown promising hypoglycemic activity. Its methanol leaves extract inhibited α-glucosidase by 83.33 ± 3.20% at 25 µgGAE/mL, exceeding the inhibition of acarbose (54.85 ± 1.48%) (Ratnadewi et al. 2020). However, the antidiabetic bioactive constituents have not yet been explored.

Thymelaceae

Phaleria macrocarpa Boerl., locally known as '*mahkota dewa'*, is a famous Indonesian native medicinal plant belonging to the Thymelaceae family. The local people usually use the fruits and leaves to treat several diseases including diabetes mellitus (Ali et al. 2012). An in vitro evaluation of *P. macrocarpa* fruit peels ethanolic extract showed its significant α-glucosidase inhibitory activity with an IC_{50} value of 1.60 ± 0.04 mg/L which is notably more potent than acarbose (IC_{50} = 55.84 mg/L) (Irawan et al. 2022). Nevertheless, no further bioprospecting was conducted to obtain the biomarker compounds.

Verbenaceae

In the Verbenaceae family, phytochemical investigation of *Lantana camara* L. aerial part led to the isolation of oleanane triterpenes along with several known flavones (Abdjul et al. 2017). Twenty-five compounds were examined for inhibitory activity against protein tyrosine phosphatase 1B (PTP1B), an enzyme which regulates insulin and leptin signalling. Seventeen potential PTP1B inhibitors (Fig. 8), in comparison to standard oleanolic acid (IC_{50} = 1.3 µM), were highlighted including 24-hydroxylantadene B **48** (IC_{50} = 7.3 µM), 3*β*-hydroxyantadene C **49** (IC_{50} = 7.3 µM), icterogenin **50** (IC_{50} = 11 µM), 4-epi-hederagonic acid **51** (IC_{50} = 8.1 µM), oleanolic acid **52** (IC_{50} = 2 µM), 22*β*-oleanolic acid **53** (IC_{50} = 7.9 µM), 3*β*-hydroxylantadene A **54** (IC_{50} = 7.2 µM), 3*β*-hydroxylantadene B **55** (IC_{50} = 5.1 µM), 22-hydroxyoleanonic acid **56** (IC_{50} = 6.9 µM), lantadene B **57** (IC_{50} = 5.5 µM), lantadene A **58** (IC_{50} = 5.2 µM), lantadene D **59** (IC_{50} = 7.9 µM), pomonic acid **63** (IC_{50} = 10.5 µM), pomolic acid **64** (IC_{50} = 10.6 µM), lantanilic acid **60** (IC_{50} = 7.5 µM), camaric acid **61** (IC_{50} = 5.1 µM), lantanolic acid **62** (IC_{50} = 13 µM) (Fig. 15) (Abdjul et al. 2017). While the remaining compounds exhibited moderate to low inhibitory activity with IC_{50} values ranging from 16 to 33 µM. Compounds **51**, **52**, and **62** demonstrated that oxidation at C-3, hydroxylation at C-24, and an ether linkage between C-3 and C-25 were unfavourable for PTP1B inhibition. These findings are consistent with earlier studies reporting that *L. camara* ameliorated HbA1c levels and body weight profiles. (Venkatachalam et al. 2011).

In vivo studies on Indonesian antidiabetic medicinal plants

In vivo testing is an important step in preclinical drug discovery, offering comprehensive insights into how drug leads interact with the dynamic and complex systems of living organisms (Hefti 2008). These models are also instrumental in predicting human responses to novel treatments (Ioannidis 2012). To

Table 2 In vivo antidiabetic studies on Indonesian medicinal plants

Family	Species	Part of plant	Extract type	Experimental Animal	Induction of diabetes	Standard drug	Dose	Effctive dose	Reduction	Time	Ref.
Acanthaceae	*Andrographis paniculata* (Burm.f.) Wall. ex Nees	Leaves	Ethanol extract	Mice	Streptozotocin	Metformin 45 mg/kg				21 days	Mardiansyah (2020)
Acoraceae	*Acorus calamus* L	Radix/roots	Ethyl acetate fraction	C57BL/Ks db/db mice	-	10 mg/kg rosiglitazone	100 mg/kgBW ACE	100 mg/kgBW	ROS 70.1%, ACE 54.5% of serum glucose	21 days	Wu et al. (2009)
Alliaceae	*Allium chinense* G.Don	Bulbs	Ethanol extract	*Rattus norvegicus* L	alloxan	Metformin 45 mg/kg BW	250, 500, 750 mg/kgBW	500 mg/kgBW	Liver histopathology	14 days	Rahmah et al. (2021)
	Allium sativum L	Bulbs	Ethanol extract	Wistar rats	Alloxan	Novomix Insulin analog 0.7 U/kgBW	3, 6, and 12 mg/200 gBW	Not significant	Not significant	1 day	Cahya et al. (2015)
Anacardiaceae	*Mangifera indica* L	Leaves	Ethanol extract	Male mice (Mus musculus)	Alloxan	Glibenclamide	18.375 and 36.75 mg/30 gBW	36.75 mg/30 gBW	54.21% dose 36.75 Glibenclamide 63.06%	14 days	Emelda et al. (2015)
Annonaceae	*Annona muricata* L	Peels	Ethanol extract	Rattus norvegicus L	Alloxan	Metformin 9 mg/kg BB	50, 75 and 150 mg/kgBW	150 mg/kgBW	25.33% (metformin) 29.33% (150 mg/kg)	10 days	Sarbunan et al. (2021)
Apiaceae	*Centella asiatica* (L.) Urb	Leaves	Ethanol extract	Zebrafish *Danio rerio*	Alloxan	Mmetformin 25 mg/2 L	100 and 200 mg/2 L Self-Nanoemulsifying Drug Delivery Systems (SNEDDS) Pegagan leaf extract (PLE)	100 mg/kgBW 4 folds	65.50% (metformin) 69.90% (100) 72.20% (200)	12 h	Hayati et al. 2021b)
Asteraceae	*Enhydra fluctuans*	Aerial	Ethanol extract	Male wistar albino	Alloxan	Glibenclamide 0.45 mg/kg	250, 500, and 1000 mg/kgBW	500	29.39 ± 6.72% (500) 35.15 ± 8.13% (gliben)	3 h	Delfita et al. (2020)
	Gynura procumbens (Lour.) Merr	Leaves	Water extract	Male Sprague–Dawley (SD) rats	Streptozotocin	Metformin 500 mg/kg	500 or 1,000 mg/kgBW	1000	29% (1000) and 49% (metformin)	14 days	Hassan et al. (2010)
	Tithonia diversifolia (Hemsl.) A.Gray	Leaves	Ethanol extract (70%)	Sprague dawley rats	Alloxan	Metformin	200, 400, and 600 mg/kgBW	600	81.87 ± 4.38 (600) 75.99 ± 9.67 (metformin)	16 days	Yazid et al. (2021b)

Table 2 continued

Family	Species	Part of plant	Extract type	Experimental Animal	Induction of diabetes	Standard drug	Dose	Effctive dose	Reduction	Time	Ref.
Menispermaceae, Caricaceae & Poaceae	Brotowali (*Tinospora crispa* (L.) Hook. f. & Thomson) and Papaya (*Carica papaya* L.) and Sugarcane (*Saccharum officinarum* L.) as mixture (EBPT)	All parts, Leaves and stem	Water juice	mice (Mus musculus)	Alloxan	Insulin analog	250 and 500 mg / kgBW	500	16% (insulin analog) 15% (500)	5 days	Purnamasari and Rusdianto (2021)
Cucurbitaceae	*Sechium edule* Sw	Fruit	Ethanol extract, ethyl acetate fraction	Albino rats	Streptozotocin and nicotinamide	Metformin 40.5 mg/kg	ethanol extract 45, 100, 150 mg/ kgBW ethyl acetate fraction 45, 100, 150 mg/kgBW	ethyl acetate fraction 100 mg/kg nearly 2.5 folds	ethyl acetate fraction 100 (64%) metformin 60%	28 days	Siahaan et al. (2021)
Fabaceae	*Glycine max* (L.) Merr	Seeds	Aqueous extract	Winstar Rat (*Rattus novergicus*)	Multi Low Dose Streptozotocin (MLD-STZ)	Not available	500, 750, 1000 mg/ kgBW	750	65%	14 days	Gina et al. (2014)
Gnetaceae	*Gnetum gnemon* L	Seeds	Ethanol extract	Male C57/BL6 mice	Streptozotocin	Not available	2% of powdered extract	–	extract did not change the plasma glucose levels	21 dyas	Ota et al. (2013)
Lamiaceae	*Clerodendrum fragrans* Willd	Leaves	Ethanol extract, ethyl acetate extract	White male rat (*Rattus novergicus*)	Alloxan	Metformin 125 mg/kg	100, 200, 300 mg/ kgBW	100	Reduced to 75.66 ± 3.18 mg/ dL (no initial blood glucose level data)	14 days	Simorangkir et al. (2022)
	Orthosiphon tamineus Benth	Roots and leaves	Ethanol extract	Mice (*Mus musculus*)	Alloxan	Not available	35 and 50 mg/20 g BW/day	Leaves extract of 50 mg/20 gBW	41.6%	7 days	Andriaty et al. (2019)
Leguminosae	*Clitoria ternatea* L	Flowers	Protein extract	male ddY mice	Alloxan	Metformin 100 mg/kg	100 and 500 mg/ kgBW	500	55% Metformin 69%	30 days	Siahaan et al. (2021)

Table 2 continued

Family	Species	Part of plant	Extract type	Experimental Animal	Induction of diabetes	Standard drug	Dose	Effctive dose	Reduction	Time	Ref.
Lythraceae	*Lawsonia inermis* L	Leaves	Hexane extract, ethyl acetate extract, ethanol extract, water extract and water infusion extract	male Wistar rats	Streptozotocin	Metformin 500 mg/kgBW	1000 mg/kgBW	Ethyl acetate extract 1000 mg/kg	36.5 ± 16% on the 3 h observation 77.9% meformin after 3 h	7 h	Widyawati et al. (2019)
Malvaceae	*Abelmoschus esculentus* (L.) Moench	Fruit	Aqueous extract	Male Swiss–Webster mice	Deficiency: alloxan Resistance: lipid emulsion	Deficiency: glibenclamide 0.65 mg/kg BW) Resistance: metformin 135 mg / kgBW	both 25 mg/kgBW, 50 mg/kgBW, 100 mg/kgBW, and 200 mg/kgBW	Deficiency: 50 76 times Resistency: 50 and 100	Def: Gliben 67% 50 mg / kg bw 73% Resistance: 50 and 100 mg/kg bw 64% and 71% respectively (insulin sensitivity increase) Metformin: 78%	Both: 14 days	Aligita et al. (2019)
		seed	Steeping coffee from okra Oligomeric catechin (3,4 mg/g)	Mice	Alloxan	Not available	1.82, 3.64 and 5.46 mg/gBW/day	5.46 mg/gBW	47.7%	10 days	Munawwarah et al. (2019)
		Fruit	Ethanol extract	male Wistar rats	Alloxan	Novomix (insulin analog) 0,4 IU/100 gBW	75 mg/kgBW/day, 150 mg/kgBW/day, dan 300 mg/kgBW/day	No effective dose	okra extract can not reduce elevated blood glucose levels on Wistar rats	1 day	Prakoso et al. (2016)
Meliaceae	*Swietenia mahagoni* (L.) Jacq	Seeds	Ethanol extract	Rat	Sucrose	Acarbose 4.5 mg/kgBW	100, 200, 300, 400, and 500 mg/kgBW	None	Normal blood glucose levels for rats was maintained ranging between 90–142 mg/dL	2 h	Wresdiyati et al. (2015)
Menispermaceae	*Tinospora crispa* L	Stem	70% Ethanolic extracts	Wistar rat	Alloxan	Glibenclamide 0.63 mg/kgBW	500, 1000 and 2000 mg/kgBW	500	44.78% Glibenclamide: 39.43%	10 days	Sutrisna et al. (2018b)

Table 2 continued

Family	Species	Part of plant	Extract type	Experimental Animal	Induction of diabetes	Standard drug	Dose	Effctive dose	Reduction	Time	Ref.
Myrtaceae	*Syzygium polyanthum* (Wight) Walp	Leaves	Methanol extract	Sprague Dawley rats (male)	Streptozotocin	Metformin 500 mg/kgBW	125, 250, 500 and 1000 mg/kgBW	250, 500, 1000 mg/kg showed antidiabetic activity in dose dependent manner comparable to metformin	Roughly 40–60% Metformin about 60%	6 days	Widyawati et al. (2015)
Oleaceae	*Olea europaea* L	Leaves	Aquous extract	Wistar rats	Alloxan	Not available	540, 1080, 2160 mg / 200 gBW	2160	53.14%	3 days for the alloxan	Millati et al. (2019)
Oxalidaceae	*Averrhoa bilimbi* L	Leaves	Ethanol extract	Male wistar rats	Streptozotocin	Glibenclamide	15 mg	15 mg	42.16% Gliben: 51.07%	10 days	Wahyuni (2021)
Ranunculaceae	*Nigella sativa* L	Seeds	Ethanol extract	Male wistar rats	Fructose	Metformin	24, 48 and 96 mg/kgBW		No significant elevation effect of insulin sensitivity	30 days	Panggabean et al. (2014)
Rosaceae	*Malus domestica* (Suckow) Borkh	Leaves	Ethanol extract (70%)	Sprague dawley rats	Alloxan	Metformin	200, 400, and 600 mg/kgBW	200	57.52 ± 9.67% (200 mg/kgBW) 75.99 ± 9.67% (metformin)		Yazid et al. (2021b)
Rubiaceae	*Morinda citrifolia* L	Fruits	Ethanol extract	Male white rats	Streptozotocin	glibenclamide 5 mg/kgBW	10, 20, 40 mg/kgBW	20	Blood glucose decrease: 48.3% Insulin increase: 55.6% Glibenclamide: 47.3% and 45.6%	7 days	Sinulingga et al. (2018)
Scrophulariaceae	*Picria fel-terrae* Lour	Leaves	Ethanol extract	Rats	Alloxan	Lantus insulin 1 unit	200 and 300 mg/kgBW	300	72.28% Insulin: 66.2%	28 days	Widjaja et al. (2017)

date, several Indonesian medicinal plants traditionally used for diabetes management have been investigated for their antidiabetic activities through *in vivo* studies (Table 2). This review outlines 30 plant species from 26 botanical families that exhibit potential antidiabetic activity. Most of the in vivo studies employed crude extracts, while only two utilised plant fractions. Leaves were the most commonly used plant part, followed by roots, bulbs, peels, aerial parts, stems, fruits, seeds and flowers. Various solvents were used to prepare the crude extracts, with ethanol (67.86%) being the most common, followed by water (21.42%) and others (10.72%). The reviewed studies used animal models such as rats, mice and zebrafish. Diabetes was typically induced using alloxan and streptozotocin and theexperimental duration varied from 2 h to 30 days. These in vivo studies primarily assessed the plants' ability to reduce blood glucose levels and enhance insulin sensitivity. Seven plant species from seven different families showed superior antidiabetic potentials compared to standard drugs used in the respective studies.

Centella asiatica (L.) Urb.

An in vivo study by Hayati et al. (Hayati et al. 2021a) evaluated the fasting blood glucose (FBG) lowering effect of an ethanolic extract of *Centella asiatic*a (L.) Urb. leaves in zebrafish induced with alloxan and pretreated with 2% glucose solution for seven days. The leaves extract was formulated in a Self-NanoEmulsifying Drug Delivery System (SNEDDS) to improve its bioavailability (Hayati et al. 2021a). The study was conducted on five groups consisting of two groups of zebrafish treated with different doses (100 and 200 mg/2 L) of the *C. asiatica* ethanol extract SNEEDS groups, the positive and negative control groups, and the standard drug group which were observed for 12 h. Both doses demonstrated better FBG reduction of 69.90% and 72.20%, respectively, compared to 50 mg/L metformin as the standard drug (Hayati et al. 2021a).

Tithonia diversifolia (Hemsl.) A.Gray.

Among three species from the Asteraceae family, only the ethanolic leaves extract of *Tithonia diversifolia* (Hemsl.) A.Gray. showed significant FBG lowering effects (Yazid et al. 2021a). At a dose of 600 mg/kg, it reduced FBG by 81.87% in alloxan-induced Sprague Dawley rats during 16 days of treatment, showing a better reduction compared to metformin as the standard drug. However, the study did not disclose the dose of metformin used, which limits the ability to perform a comprehensive analysis of the results (Yazid et al. 2021a). Furthermore, histological examination showed pancreatic tissue repairment with small-sized Langerhans islets and dominated by β-cells as compared to the normal, positive and negative control groups, suggesting protective effects against liver complications (Yazid et al. 2021a).

Sechium edule Sw.

Sechium edule Sw. (Cucurbitaceae), also known as chayote squash, has pharmacological effects as antidiabetic, antioxidant, anti-inflammatory, anti-obesity, anticancer, and hepatoprotective agents. Siahaan et al. (2021) reported the effects of its fruit ethanolic extract and ethyl acetate fraction in streptozotocin and nicotinamide induced albino rats. The ethyl acetate fraction at the dose of 100 mg/kg significantly reduced blood glucose levels by 60%, comparable to 40.5 mg/kg of metformin (60%) (Siahaan et al. 2021). This study alsoindicated that treatment with 100 mg/kg of ethanolic *Sechium edule* Sw. Fruit extract could stimulate insulin secretion and help protect pancreatic β-cells from degeneration by reducing oxidative stress (Siahaan et al. 2021).

Abelmoschus esculentus (L.) Moench

Aligita et al. (2019) evaluated the antidiabetic activity of *Abelmoschus esculentus* (L.) Moench fruit in Male Swiss–Webster mice models of insulin deficiency and insulin resistance. Commonly known as okra, this plant is one of the most widely used species in the Malvaceae family. Results showed that in the insulin deficiency group, oral administration of aqueous of *A. esculentus* fruit extract at concentration of 25, 50, 100 and 200 mg/kg resulted in reductions of blood glucose levels by 38%, 73%, 72%, and 64%,, respectively, after two weeks of treatments. Among these, the 50 mg/kg dose displayed the most remarkable blood glucose-lowering effect, closely comparable to that ofthe standard drug glibenclamide (0.65 mg/kg), which produced a 67% reduction in blood glucose levels (Aligita et al. 2019). In the insulin resistance

group, treatment with the *A. esculentus* fruit aqueous extract at doses of 50 and 100 mg/kg significantly improved insulin sensitivity, with increases of 64% and 71%, respectively. The antidiabetic activity of *A. esculentus* fruit was attributed to enhanced insulin secretion and sensitivity, as well as the inhibition of intestinal carbohydrate absorption (Aligita et al. 2019).

Tinospora crispa L.

Tinospora crispa L. (Menispermaceae), commonly found growing wild in forests or cultivated in home gardens, is widely used in traditional Indonesian medicine to treat diabetes mellitus (Sutrisna et al. 2018a). The stem of *T. crispa* was extracted using 70% ethanol and reported to exhibit hypoglycemic effect in diabetic Wistar rats previously induced with alloxan. Administration of the extract at a dose of 500 mg/kg resulted ina 44.78% reduction in fasting blood glucose (FBG) levels. This dose produced the most significant glucose-lowering effect compared to higher doses (1000 and 2000 mg/kg) and was even more effective than the standard drug glibenclamide (0.63 mg/kg), which achieved a 39.43% reduction (Sutrisna et al. 2018b). Furthermore, histopathological examination of the pancreatic tissue from treated diabetic rats showed the absence of necrotic islet cells, indicating that the ethanolic stem extract of *T. crispa* may support the regeneration or protection of pancreatic islet cells (Sutrisna et al. 2018b).

Morinda citrifolia L.

Another study conducted on streptozotocin-induced diabetic male white rats demonstrated that the ethanolic extract of *Morinda citrifolia* L. fruits effectively lowered plasma glucose levels by increasing insulin secretion (Sinulingga et al. 2018). Diabetic rats were administered the extract at doses of 10, 20, 40 mg/kg, alongside a standard group treated with glibenclamide (5 mg/kg). Fasting plasma glucose levels and insulin secretion were monitored for seven days. Among the treatment groups, the 20 mg/kg dose of *M. citrifolia* L. fruit extract significantly reduced plasma glucose levels (48.3%) as compared to negative controls and was higher than the standard drug glibenclamide 5 mg/kg (47.3%) (Sinulingga et al. 2018). Similarly, this dose also induced the most significant increase in insulin secretion, with a 55.6% elevation compared to the control group. The study attributed the antidiabetic activity of *M. citrifolia* to various bioactive compounds such as flavonoids, saponins, triterpenoids and triterpenes (Sinulingga et al. 2018).

Picria fel-terrae Merr

Picria fel-terrae Merr., a member of the Scrophulariaceae family, is widely distributed across Indonesia, including North Sumatra. It has been empirically used for treating diseases such as cancer, diabetes melitus, fever and malaria for years (Widjaja et al. 2017). In an in vivo study, Widjaja et al. (2017) evaluated the antidiabetic activity of the ethanolic extract of *P. fel-terrae* leaves in alloxan- induced diabetic rats. The results revealed that administration of the extract at doses of 200 and 300 mg/kg effectively reduced blood glucose levels, with the 300 mg/kg dose demonstrating a more pronounced effect than the 200 mg/kg dose.. Furthermore, the 300 mg/kg dose of the ethanolic extract achieved a 72.28% reduction in blood glucose levels, surpassing the effect of the standard drug insulin, which produced a 66.2% reduction. (Widjaja et al. 2017).

Clinical studies of Indonesian antidiabetic medicinal plants

The indigenous people of Indonesia have practiced their traditional herbal medicine, known as *Jamu*, for centuries. Jamu is commonly prepared as decoctions or packed in a modernised form into capsules and tablets. Due to the long-term clinical uses of Jamu, the ingredients used were categorised as non-toxic products. Because of this established safety profile, the Indonesian government classifies many *Jamu* ingredients as non-toxic and low risk. Consequently, only well-known and traditionally used *Jamu* formulations are subject to simplified regulatory oversight, allowing them to proceed directly to clinical trials without extensive preclinical testing. A number of medicinal plants commonly used in *Jamu* have been prescribed to diabetic patients, and their effects on blood glucose levels have been clinically evaluated. These plants include, *Piper crocatum*, *Moringa oleifera*, *Muntingia Calabura* L., *Swietenia mahagoni*, *Cinnamomum burmanii*, *Phaleria macrocarpa*, *Pandanus*

amaryllifolius roxb, *Syzygium polyanthum*, *Andrographis paniculata*, *Curcuma xanthoriza*.

Piper crocatum

Piper crocatum contains various bioactive compounds, including alkaloids, flavonoids, saponins, tannins and essential oils. Among these, flavonoids and alkaloids are believed to possess hypoglycaemic properties, potentially contributing to blood glucose reduction (Safithri and Fahma 2008; Suri et al. 2021). In one study, a 70% ethanol extract of *P. crocatum* leaves was administered to Wistar rats induced with diabetes mellitus (DM) using streptozotocin over a 21-day period. Rats treated with 50, 100, and 200 mg/kg body weight/day of the extract showed a significant reduction in fasting blood glucose levels compared to the control group, suggesting the antidiabetic potential of *P. crocatum* (Andhi 2016). Another study evaluated the effect of P. *croratum* leaf decoction in alloxan-induced diabetic Sprague Dawley rats. After 10 days of daily administration at various doses, blood glucose levels were reduced by 10–38%. These findings further support the antihyperglycemic activity of *P. crocatum* in animal models.

A pre-post quasi-experimental study conducted in Madura, Indonesia, discovered that the use of *Piper crocatum* decoction significantly reduced blood glucose levels in patients with type II DM (T2DM). In this study, three *P. crocatum* leaves were boiled in approximately ± 600 mL of water until the volume was reduced by half (± 300 mL). Participants consumed approximately 100 mL of the decoction once daily after meals. The study was carried out in April 2017 and involved 18 adult T2DM patients aged 41–60 years, recruited from the Batuporo sub-district of Madura. Data were analysed using the paired sample T-test, and the results showed a statistically significant reduction in fasting blood glucose levels following the intervention. The mean blood glucose level decreased from 244.56 ± 28.73 mg/dL to 231.17 ± 28.88 mg/dL ($p < 0.000$) (Widiyono and Suwarni 2019).These findings, along with results from other in vivo and clinical studies, support the potential of *P. crocatum* as a supplementary herbal remedy to aid in the management and maintenance of normal blood glucose levels in diabetic patients.

Moringa oleifera Lam.

Moringa oleifera, a member of the *Moringaceae* family, is known as a nutrient-dense plant due to the high abundance of essential phytochemicals, vitamins, and micronutrients found in its leaves, pods, and seeds (Kasolo et al. 2010; Mbikay 2012; Rockwood et al. 2013). The leaves of *M. oleifera* contain a range of bioactive compounds, including alkaloids, saponins, phytosterols, tannins, polyphenols, sterols, phenolics, and flavonoids. These constituents exhibit strong antioxidant properties and are believed to contribute to its anti-cholesterol effect (Berkovich et al. 2013). Moreover, *M. oleifera* contains anti-cancerous substances such glucosinolates, isothiocyanates, glycoside compounds, and glycerol 1-(9-octadecenoate). The flavonoids present in Moringa leaves have been shown to exhibit both antidiabetic and antioxidant activities, offering potential therapeutic benefits for individuals with hypercholesterolemia and hyperglycaemia (Gupta et al. 2012; Mbikay 2012).

A quasi-experimental study conducted in the Pakong sub-district of Madura, Indonesia, demonstrated that *M. oleifera* leaf powder significantly reduced blood glucose and cholesterol levels in participants. The study involved 40 obese adults (BMI > 25) aged between 18 and 40. Exclusion criteria included athletes, pregnant and breastfeeding women, and individuals taking medications such as antibiotics or weight-loss drugs. Participants were randomly assigned to either a treatment group or a control group. The treatment group received 500 mg of *Moringa* leaf powder daily, while the control group received only educational sessions on the prevention of hyperglycemia and hypercholesterolemia. Results showed a statistically significant reduction in mean fasting blood glucose levels in the treatment group, from 132.5 ± 42.1 mg/dL before the intervention to 119.4 ± 30.2 mg/dL after the intervention ($p = 0.009$). In contrast, the control group showed no significant change (pre-intervention: 178.1 ± 24.4 mg/dL; post-intervention: 175.95 ± 24.9 mg/dL; $p > 0.550$) (Denta et al. 2022). These findings are supported by a study conducted by Syamra et. al (2018), which reported that *M. oleifera* leaf decoction effectively reduced blood glucose levels in diabetic patients (Arleni and Andi 2018).

The flavonoids and alkaloids present in *M. oleifera* leaves contribute to itshypoglycaemic effects by promoting pancreatic β-cell regeneration and stimulating insulin release through both intra pancreatic and extra pancreatic mechanisms. Specifically, alkaloids are believed to stimulate sympathetic neurons, thereby increasing insulin release (Larantukan et al. 2014). Moreover, Divi et al. (2012) was effective in treating both streptozotocin (STZ)-induced Type 1 diabetes and insulin-resistant Type 2 diabetes in rat models. This suggests that the antioxidants compounds in *M. oleifera* play a crucial role in mitigating the oxidative stress caused by STZ-induced damage. The flavonoids in *M. oleifera* are thought to scavenge reactive oxygen species (ROS) released by mitochondria, thus protecting β-cells and keeping hyperglycemia under control (Al-Malki and El Rabey 2015; Kamalakkannan and Prince 2006).

The study conducted in Pakong sub-district of Madura, Indonesia, also discovered that after consumption of *M. oleifera* leaves powder significantly reduced cholesterol level in study participants The mean total cholesterol level in the treatment group decreased from 187 ± 24.4 mg/dL to 173.3 ± 20.3 mg/dL ($p < 0.001$), while the reduction observed in the control group was not statistically significant (before: 184.3 ± 31.5 mg/dL; after: 182.55 ± 25.0 mg/dL; $p > 0.601$)(Denta et al. 2022). Supporting these findings, an animal study showed that treatment of *M. oleifera* leaves dose of 75 mg/kg resulted in a reduction of total blood cholesterol in rats by up to 47.5%. These results suggest that *M. oleifera* leaves powdered may serve as a natural agent for the prevention of hyperglycemia and hypercholesterolemia and may be beneficial as for diabetes mellitus and dyslipidemia.

Swietenia mahagoni (L.) Jacq.

A water decoction of *Swietenia mahogany* seeds has been traditionally used in Indonesia as a folk remedy for managing blood glucose levels (Kadota et al. 1990). Several studies have explored the therapeutic properties of *S. mahogany* seeds, examining their effects on blood glucose, insulin levels, and pancreatic tissue in diabetic animal models. The antidiabetic properties of its extract have been demonstrated through in vitro and in vivo experiments, as well as in a limited number of clinical trials (Sukardiman and Ervina 2020).

The primary phytoconstituents found in the methanolic and aqueous extracts of *S. mahogany* seeds include tannins, alkaloids, saponins, terpenoids, anthraquinones, cardiac glycosides, and volatile oils (Sahgal et al. 2009). The methanolic *S. mahogany* seed extract (MEMS) has been shown to inhibit the α-glucosidase enzyme, thereby reducing the digestion and absorption of complex carbohydrates, and involving in the repair of damaged cells. One of its bioactive constituents, swietenin acts as a PPARγ agonist, enhancing insulin secretion, promoting glucose uptake, increasing peripheral glucose utilization, and lowering blood glucose levels in diabetic models. Notably, the PPARγ agonist activity of *S. mahagoni* extract at the dose of 1000 mg/kg was reported to be approximately half as effective as rosiglitazone in diabetic mice (Li et al. 2005). In addition, administration of MEMS reduced blood glucose and liver glycogen levels in streptozotocin (STZ)-induced diabetic rats. It also elevated antioxidant enzyme activity and reduced free radicals levels, indicating its potential for glycemic control and managing diabetes-related complications associated such as hyperlipidaemia and oxidative stress (Ghosh et al. 2011). Similar outcomes were observed when MEMS was compared to metformin in diabetic rats, suggesting its promise as a complementary or alternative therapeutic option (Bera et al. 2012).

Meanwhile, aqueous extracts of *Swietenia mahagoni* leaves (AEML) have also showed antidiabetic properties by reducing fasting BGL in diabetic rats. Additionally, a study discovered that both aqueous (AEML) and ethanol extracts of *S. mahogoni* (EEMS) exhibited α-glucosidase inhibitory activity, along with in vitro and in vivo hypoglycaemic effects at doses ranging from 100 to 500 mg/kg body weight (Wresdiyati et al. 2015; Yp and Urooj 2015).

Several studies have demonstrated the effectiveness of EEMS in reducing BGL through multiple proposed mechanisms, including boosting insulin secretion, decreasing food intake, reducing TNF-a levels, and preventing damage to pancreatic cells and the islets of Langerhans (Mahid-Al-Hasan et al. 2015; Suryani et al. 2013). In addition, Hajra et al. (2011) reported that the EEMS exhibited α-amylase inhibitory activity in vitro, supporting its antidiabetic potential. In diabetic rat models, EESM showed a

relatively stronger antidiabetic effect than the standard drug glibenclamide. Notably, Sukardiman et al. (2017) found that its glucose-lowering surpassed that of glibenclamide in a dose-independent manner. This study guided the development of *S. mahogoni* seed extract into pharmaceutical formulations, with a dried preparation composed of mahogany extract, Avicel, and Cab-O-Sil in a 70:30 ratio, subsequently dried at a 4:1 ratio (Sukardiman and Ervina 2020). The antidiabetic activity was attributed primarily to the flavonoid and saponin content of the extract. Furthermore, an increase in total haemoglobin (Hb) and a decrease in glycosylated Hb levels were observed following treatment. Histological and biochemical analyses of the pancreas confirmed these findings, indicating that the extract's antidiabetic mechanism involved enhanced insulin secretion (Kalaivanan and Pugalendi 2011; Kurniawati et al. 2010).

A more recent clinical study of *S. mahagoni* was performed in 68 patients with type 2 diabetes (T2D) using an experimental pre- and post-test control group design. The results showed that 85.3% of participants in the treatment group achieved blood glucose levels within the range of 90 to 199 mg/dL. Based on bivariate analysis, *S. mahagoni* seed demonstrated significant potential in reducing BGL when compared to glimepiride (Astuti 2017).

Collectively, various extracts of *S. mahagoni* seed have exhibited antidiabetic activities through several mechanisms, including lowering BGL, suppressing α-amylase and α-glucosidase activity, restoring liver and pancreatic islet function, and possessing antioxidant and antihyperlipidemic effects.

Cinnamomum burmanni (Nees & T.Nees) Blume

Indonesian cinnamon (*Cinnamomum burmanni*), a traditionally used spice, has been extensively studied for its pharmaceutical potential and rich phytochemical constituents. Its key chemical constituents include cinnamyl alcohol, cinnamaldehyde, coumarin, cinnamic acid, anthocyanin, flavonoids and essential oils (Al-Dhubiab 2012). The active substance in cinnamon bark, particularly polyphenols from flavonoids, are known to enhance insulin sensitivity and reduce blood glucose levels by augmenting insulin receptors. However, in vitro and in vivo studies specifically validatingthese effects for *C. burmannii* remain limited.

The blood glucose-lowering mechanism of *C. burmannii* can be explained by the evidence that cinnamon polyphenol extracts exhibit insulin-like and insulin-independent effects on gene regulation in mouse adipocytes. Cao et al. (2010) investigated the effect of *Cinnamon* extract (CE) on gene expression in cultured mouse adipocytes and discovered that CE modulated the expression of adipokines, upregulated *GLUT1*, and influenced components of the insulin signaling pathway. Additionally, a study examined the effects of standardized extract combination containing *Lagerstroemia speciosa* and *C. burmannii* (DLBS3233) on glucose homeostasis in rats and insulin-resistant Wistar rats. The results demonstrated that DLBS3233 enhanced tyrosine phosphorylation of the insulin receptor substrate and upregulated genes involved in insulin signalling and sensitivity. This extract also promoted glucose uptake, increased adiponectin secretion, and decreased resistin levels (Tandrasasmita et al. 2011).

Several studies conducted in Indonesia have investigated the potential of *C. burmanni* in reducing blood glucose levels. A clinical experimental study involving 20 diabetic patients revealed a significant reduction in blood glucose levels following the consumption of *C. burmanii* bark decoction for one week (Fatmalia 2017). More recently, a study in Makassar, Indonesia, involving individuals with prediabetes found that cinnamon bark administration over 14 days significantly lowered fasting blood glucose levels (Jafar et al. 2020). In addition, a study conducted in Portugal indicated that cinnamon tea might help regulate glucose metabolism in nondiabetic adults during the postprandial period. The study observed a slight decrease in postprandial blood glucose levels, resulting in a reduced maximum glucose concentration and less fluctuation after meals (Bernardo et al. 2015). However, contrasting results were reported in arandomized controlled trial indicated that administering an aqueous cinnamon extract (6 g/100 mL) to adults with type 2 diabetes mellitus (T2D) did not significantly influence postprandial glucose response during an oral glucose tolerance test (OGTT) (Rachid et al. 2022).

Furthermore, a systematic review and meta-analysis concluded that supplementation with *C. burmanii* significantly reduced fasting blood sugar (FBS) by an average of 19.26 mg/dL), while no significant changes in other glycaemic parameters or anthropometric

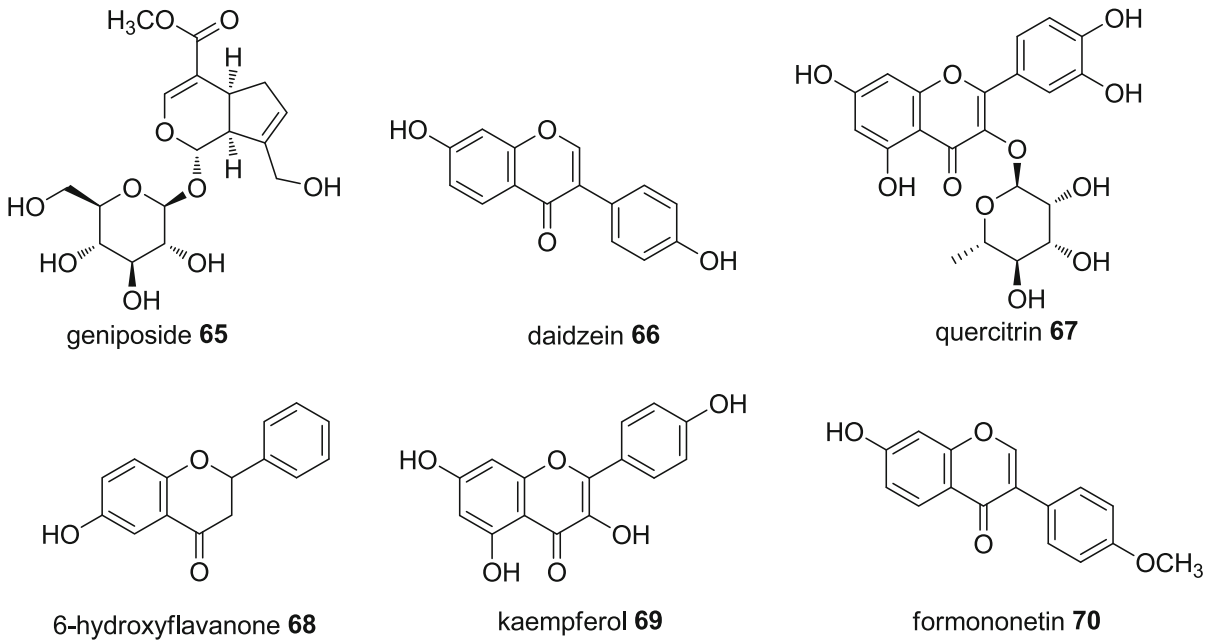


Fig. 16 Antidiabetic active constituents of Indonesian *M. calabura*

indices. Additionally, serum insulin levels and insulin resistance remained unaffected (Namazi et al. 2019).

Muntingia calabura L.

Muntingia calabura, a plant commonly found in Indonesia and other tropical regions, has been used inthe form of leaves decoction to manage diabetes. However, the hypoglycaemic activity and potential benefits of this plant in diabetes management have only been reported in a limited number of studies. An in vitro study was carried out to investigate the bioactive compounds and antidiabetic activities of *M. calabura* leaves. The extract exhibited strong α-glucosidase and α-amylase inhibitory activities. Through UHPLC-ESI–MS/MS analysis, 61 compounds were tentatively identified in the most active extract. Further quantitative analysis using UHPLC revealed that geniposide **65**, daidzein **66**, quercitrin **67**, 6-hydroxyflavanone **68**, kaempferol **69**, and formononetin **70** were the predominant constituents present in the active extract (Fig. 16) (Zolkeflee et al. 2022).

An in vivo study on hyperglycemic rats investigated the effect of *Muntingia calabura* ethanol extract (450 mg/kgBW) on blood glucose levels. The extract significantly reduces blood glucose, with results comparable to the group treated with metformin. The bioactive compounds present in *M. calabura*. L were reported to support the regeneration of pancreatic *β*-cells, enabling insulin production to help maintain normal glucose level (Andalia et al. 2021). A similar result was observed in a separate study using a water extract of *M. calabura* leaves administered at a dose of 400 mg/kgBW to insulin-deficient and insulin-resistant animal models. In the insulin-deficient model, the extract significantly reduced FBG levels, while In the insulin-resistant model, it improved the insulin tolerance constant. The study concluded that the water extract *M. carabula* leaves at 400 mg/Kg bw exerted antidiabetic activities through multiple mechanisms, including lowering blood glucose level, regenerating pancreatic *β*-cells, and enhancing insulin sensitivity (Aligita et al. 2018). The antidiabetic potential of *M. calabura* fruit (100 mg/kg) was investigated in streptozotocin (STZ)-induced diabetic rats. The study demonstrated that the fruit extract significantly reduced blood glucose levels, implying its potential as a complementary therapy alongside conventional antidiabetic drugs (Pramono and Santoso 2014). In addition, a quasi-experimental study involving 15 patients with T2D was conducted to assess the effect of *M. calabura* fruit on blood glucose levels. The results revealed a significant reduction in the patients'

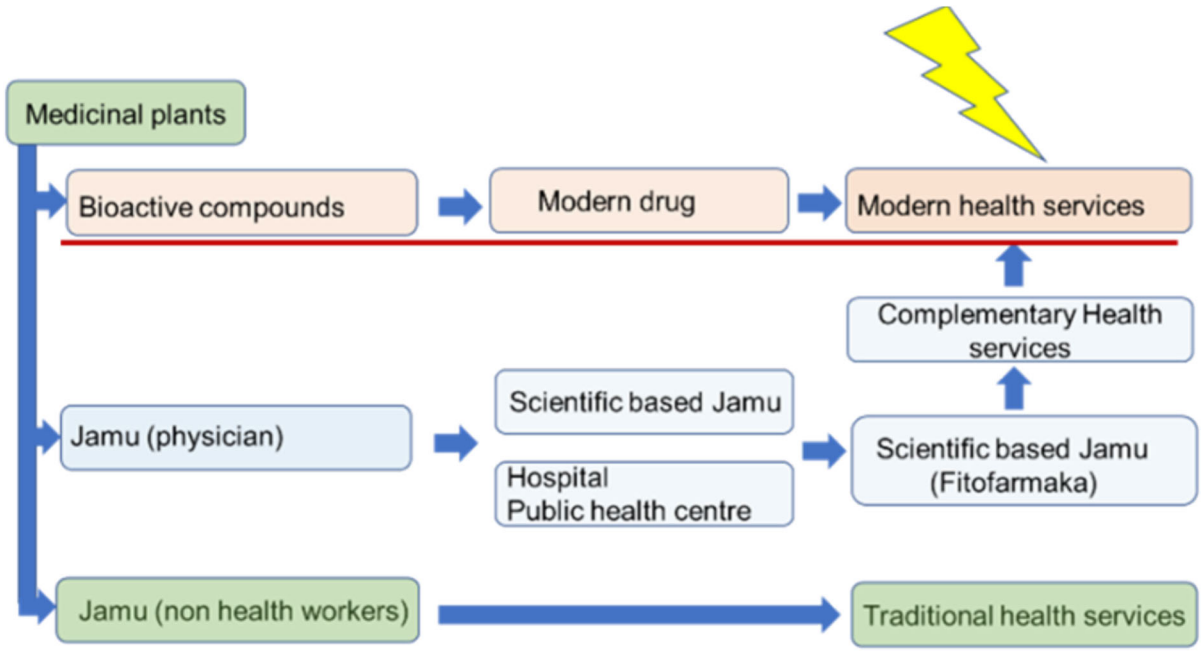


Fig. 17 Herbal medicine-based drug development in Indonesia (Rani et al. 2023)

average blood glucose levels following the intervention (Agustina and Samsul Bahri 2016).

Antidiabetic formula

An herbal-based medicine was prepared as a formula combining several plant ingredients for synergistic effects. The formulation consisted of 5 g *Syzygium polyanthum* leaves, 5 g *Andrographis paniculata* herbs, 7 g *Cinnamomum burmani* barks, and 10 g *Curcuma xanthoriza* rhizomes. A clinical study involving 242 volunteers was conducted to evaluate the formula's efficacy. Participants were divided into two groups: one received the herbal decoction twice daily, while the other was treated with oral metformin for six weeks. At baseline (day 0), the fasting blood glucose (FBG) levels were 162.92 in the decoction group and 164.37 mg/dL in the metformin group. By day 21, the average FBG levels had decreased to 155.37 mg/dL and 154.87 mg/dL, respectively. Notably, at the end of the study (day 42), the FBG level in the decoction group further decreased to 149.11 mg/dL, whereas the metformin group showed a level of 162.92 mg/dL. These results suggest that the herbal formula demonstrated a more pronounced anti-hyperglycemic effect over the medium term compared to the conventional drug treatment (Astana and Nisa 2021).

Indonesian Government policies toward modern herbal medicine regulation and development

One of the major challenges facing the pharmaceutical sector in Indonesia is its heavy reliance on imported of pharmaceutical raw materials, which accounts for approximately 90% of the total supply, with an estimated annual value of around 13 trillion rupiah (Indonesia 2015). The Covid-19 pandemic further emphasized the need for national health resilience, prompting the government to strengthen policies aimed at achieving greater self-sufficiency in healthcare services, including domestic medicine production (Indonesia 2021b). Drug development policies in Indonesia are outlined in the National Research Master Plan, which is operationalized in the National Research Priorities. One of its strategic focus areas is health, particularly in research and technology to produce medicinal preparations derived from natural raw materials. This includes the development of standardized herbal medicine ingredients and phytopharmaceutical products (Fig. 17) (Indonesia 2019). The implementation of these policies has actively encouraged research and innovation in the development of phytopharmaceuticals to support and reinforce the domestic pharmaceutical industry (Indonesia 2021a). To date, records indicate that 26

phytopharmaceutical products have successfully demonstrated their safety and efficacy through comprehensive preclinical and clinical evaluations (Indonesia 2021a).

The National Agency of Drug and Food Control in Indonesia classifies herbal medicine into three categories: *jamu*, *obat herbal terstandard* (OHT) and *fitofarmaka*. *Jamu* refers to traditional Indonesian herbal medicines whose safety and efficacy are supported by empirical use, with over 12,000 registered products currently available. *Obat herbal terstandard* (OHT) are standardized herbal medicines with scientifically validated safety and efficacy through preclinical studies, with 86 products officially registered. Meanwhile, *fitoframaka* represents the highest category of herbal medicines whose safety and efficacy have been confirmed through preclinical and clinical trials, with a total of 26 registered products as of 2021 (RI 2021). Despite Indonesia's rich biodiversity and favorable tropical climate, which provide an abundant and sustainable source of medicinal plant materials, natural product-based pharmaceuticals remain a relatively minor segment within the country's 202 pharmaceutical industries. Nevertheless, the development of *fitofarmaka* has become a national priority in the advancement of natural product-based therapeutics, particularly for chronic diseases such as diabetes. (RI 2021). To support this, the Indonesian government actively promotes research and innovation, encouraging start-ups and pharmaceutical companies to develop scientifically grounded, natural ingredient-based products capable of becoming mainstream pharmaceutical options, including *fitofarmaka* for diabetes therapy.

One of the major challenges in development of *fitofarmaka* is the prevalence of misinformation, which has led some health practitioners to dispense herbal products alongside conventional medicine without adequate scientific validation. On the other side, the Indonesian government has taken steps to promote the responsible and evidence-based use of herbal medicines through initiatives such as the establishment of *Klinik Herbal*, a dedicated herbal medicine clinic located in Karanganyar Regency-Central Java (Indonesia 2010). Managed by the Ministry of Health, this clinic serves as a platform to introduce and promote the clinical application of herbal-based medicines to both general practitioners and the wider public (Indonesia 2010). Since its establishment, the number of patients visiting Klinik Herbal has steadily increased, particularly among those seeking alternative or complementary therapies for chronic conditions such as diabetes and other metabolic disorders (Indonesia 2010). Notably, this clinic is the first of its kind in Indonesia, employing a multidisciplinary team comprising researchers, medical doctors, and pharmacists. Furthermore, it remains accessible to the public at no cost, making herbal-based healthcare services more widely available and supporting the government's efforts to integrate scientifically validated herbal medicines into national health services (Indonesia 2010).

Despite the government's development focus on *fitofarmaka,* several policies have also been established to ensure the quality and safety of other forms of herbal-based medicines, particularly *Jamu*, which remains the most widely produced and consumed traditional medicine in Indonesia, despite historically limited regulations (Indonesia 2022). To address this, the government introduced Good Manufacturing Practices for Traditional Medicines (GMP-OT)—a set of enforced production standards specifically designed for herbal medicines, including *jamu*. This protocol is tailored to small-scale production, making it suitable for local industries and even home-based enterprises (Indonesia 2022). These traditional medicine industries play a significant role in the national economy, employing millions of people (Makanan 2023). However, one of the primary challenges faced by small-scale producers is maintaining hygiene standards, with approximately 80% of these industries reportedly encountering issues in this area. In response, the government has provided incentives, training programs, and technical support to help improve hygiene practices and production quality. Financial assistance and facilitation have also been made available to ease the financial burden on small enterprises in meeting these standards (Makanan 2023).

Overall, alongside these regulatory and capacity-building efforts, the government continues to actively encourage research aimed at the discovery and development of new phytopharmaceuticals, with the long-term goal of positioning them as a leading component of the country's pharmaceutical sector.

Conclusions

Diabetes remains one of the major public health burdens in Indonesia. Due to limited accessibility, affordability, and sometimes limited effectiveness of conventional Western medicines, many Indonesians continue to rely on traditional and herbal remedies for managing various types of diabetes, especially T2D. Numerous scientific studies have demonstrated that these medicinal plants exhibit a wide range of antidiabetic activities, from mild to potent effects. In in silico studies, compounds such as gartanin, quinidine, and quinine have been identified as promising SIRT1 activators with potential antidiabetic properties. Furthermore, both in vitro and in vivo investigations have revealed strong antidiabetic activities in plant species such as *Cordia myxa, Merremia mammosa, Antidesma bunius, Antidesma montanum, Lunasia amara, Phaleria macrocarpa.* Several traditional herbal formulations from the mixture of *Centella asiatica, Tithonia diversifolia, Sechium edule* Sw., *Abelmoschus esculentus, Tinospora crispa, Morinda citrifolia, Picria fel-terrae* have also demonstrated notable antidiabetic activities. Interestingly, several medicinal plants, including *Piper crocatum, Moringa oleifera, Muntingia Calabura L., Swietenia mahagoni, Cinnamomum burmanii, Phaleria macrocarpa, Pandanus amaryllifolius roxb, Syzygium polyanthum, An-drographis paniculata, Curcuma xanthoriza* have been tested in the health clinics involving small groups of diabetic patients, These trials reported significant improvements in glycemic control, highlighting their potential as alternative therapeutic options for T2D management. Despite these promising findings, many Indonesian medicinal plants with potential antidiabetic properties remain unexplored. In response, the Indonesian government has recently introduced updated regulations, supportive policies, and increased research funding to encourage the systematic exploration, validation, and development of these traditional resources into scientifically based modern medicines.

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Data availability The data that supports the findings of this study were available upon reasonable request from the corresponding author.

Declarations

Conflict of interest All authors declare no competing interest.

References

Abdjul DB, Yamazaki H, Maarisit W, Rotinsulu H, Wewengkang DS, Sumilat DA, Kapojos MM, Losung F, Ukai K, Namikoshi M (2017) Oleanane triterpenes with protein tyrosine phosphatase 1B inhibitory activity from aerial parts of *Lantana camara* collected in Indonesia and Japan. Phytochemistry 144:106–112

Agustina A, Samsul Bahri T (2016) Pengaruh pemberian *Muntingia calabura* L. terhadap kadar glukosa darah pada pasien DM type II di Aceh Besar. Jurnal Ilmiah Mahasiswa Keperawatan 1(1):1–5

Al-Dhubiab B (2012) Pharmaceutical applications and phytochemical profile of *Cinnamomum burmannii*. Pharmacogn Rev 6:125–131

Al-Malki AL, El Rabey HA (2015) 'The antidiabetic effect of low doses of *Moringa oleifera* lam seeds on streptozotocin induced diabetes and diabetic nephropathy in male rats. BioMed Res Int 2015:1–14

Ali RB, Atangwho IJ, Kuar N, Mohamed EA, Mohamed AJ, Asmawi MZ, Mahmud R (2012) Hypoglycemic and antihyperglycemic study of *Phaleria macrocarpa* fruits pericarp. J Med Plants Res 6(10):1982–1990

Aligita W, Muhsinin S, Susilawati E, Dahlia Pratiwi, D. S., Aprilliani, D., Artarini, A. and Adnyana, I. K. (2019) Antidiabetic activity of okra (*Abelmoschus esculentus* L.) fruit extract. Rasayan J Chem. 12(1):157–167

Aligita W, Susilawati E, Sukmawati IK, Holidayanti L, Riswanti J (2018) Antidiabetic activities of *Muntingia calabura* L. leaves water extract in type 2 diabetes mellitus animal models. Indones Biomed J 10(2):165–170

Almurdani M, Fikriyah M, Zamri A, Nugroho TT, Jasril J, Eryanti Y, Teruna HY (2020) Antidiabetic activity of some extracts from *Anisophyllea disticha* leaves. J Phys Conf Ser 1655(1):012032

A American Diabetes (2020) Classification and diagnosis of diabetes: standards of medical care in diabetes—2020. Diabetes Care 43(Supplement_1):S14–S31

Andalia N, Nur Salim M and Balqis U (2021) Decreasing blood glucose levels using *Muntingia calabura* L. leaf extract in rats with diabetes mellitus, translated by Faculty of Veterinary Medicine, Universitas Syiah Kuala: Atlantis Press., 179–183.

Andhi S (2016) Antidiabetic and antioxidant activities of 70% ethanol-diluted extract of *Piper Crocatum* Leaves in Stretozotocin induced diabetic rats sktifitas sntidiabetik dan sntioksidan extract etanol 70% daun Sirih Merah (*Piper crocatum*) pada tikus Wistar model diabetes mellitus. Jurnal Kedokteran Brawijaya 29(1):1–4

Andriaty SN, Akbar F, Wahab A (2019) Perbandingan efektifitas ekstrak etanol 96% akar dan daun Kumis Kucing (*Orthosiphon stamineus*) terhadap penurunan glukosa darah mencit (*Mus Musculus*). Jurnal Ilmu Kedokt Dan Kesehat 6(4):296–303

Arleni S, Andi I (2018) Pemberian rebusan daun Kelor terhadap penurunan kadar glukosa darah pada pasien penderita diabetes mellitus (Dm). Jurnal Media Laboran 8(2):50–55

Arsiningtyas IS, Gunawan-Puteri MD, Kato E, Kawabata J (2014) Identification of alpha-glucosidase inhibitors from the leaves of *Pluchea indica* (L.) Less., a traditional Indonesian herb: promotion of natural product use. Nat Prod Res 28(17):1350–1353

Association AD (2020) Pharmacologic approaches to glycemic treatment: standards of medical care in diabetes—2020. Diabetes Care 43(Supplement_1):S98–S110

Astana PRW, Nisa U (2021) The effect of Indonesian anti-hyperglycemic herbal formula on fasting blood glucose and quality of life of diabetic patients: a randomized, open-label clinical trial. Trop J Nat Prod Res 5(7):1265–1270

Astuti A (2017) Biji mahoni (*Swietenia mahagoni*) menurunkan glukosa darah pada diabetes melitus tipe II. Jurnal Ipteks Terap 11(3):187–187

Aziz Z, Yuliana ND, Simanjuntak P, Rafi M, Mulatsari E, Abdillah S (2021) Investigation of Yacon leaves (*Smallanthus sonchifolius*) for α-glucosidase inhibitors using metabolomics and *in silico* approach. Plant Foods Hum Nutr 76(4):487–493

Azminah A, Erlina L, Radji M, Mun'im A, Syahdi RR, Yanuar A (2019) *In silico* and *in vitro* identification of candidate SIRT1 activators from Indonesian medicinal plants compounds database. Comput Biol Chem 83:107096

B2P2TOOT (2012) Laporan nasional eksplorasi pengetahuan lokal etnomedisin dan tumbuhan obat di Indonesia berbasis komunitas, Ministry of Health Republic of Indonesia.

B2P2TOOT (2015) Laporan nasional eksplorasi pengetahuan lokal etnomedisin dan tumbuhan obat di Indonesia berbasis komunitas.

B2P2TOOT (2017) Laporan nasional eksplorasi pengetahuan lokal etnomedisin dan tumbuhan obat di Indonesia berbasis komunitas.

Bakri R, Wijayanto H, Afendi FM (2016) Prediksi senyawa aktif pada tanaman obat berdasarkan kemiripan struktur kimiawi untuk penyakit diabetes tipe II. Jurnal Jamu Indones 1(3):1–5

Bera TK, Chatterjee K, Jana K, Ali KM, De D, Maiti S, Ghosh D (2012) Antihyperglycemic and antioxidative effect of hydro - methanolic (2:3) extract of the seed of *Swietenia mahagoni* (L.) Jacq. in streptozotocin-induced diabetic male albino rat: an approach through pancreas. Genomic Med, Biomarkers, Health Sci 4(4):107–117

Berkovich L, Earon G, Ron I, Rimmon A, Vexler A, Lev-Ari S (2013) *Moringa oleifera* aqueous leaf extract down-regulates nuclear factor-kappaB and increases cytotoxic effect of chemotherapy in pancreatic cancer cells. BMC Complement Altern Med 13:212

Bernardo MA, Silva ML, Santos E, Moncada MM, Brito J, Proença L, Singh J, De Mesquita MF (2015) Effect of Cinnamon tea on postprandial glucose concentration. J Diabetes Res 2015:1–6

Cahya BP, Mambo C, Wowor MP (2015) Uji Efek Ekstrak Umbi Bawang Putih (*Allium Sativum* L.) terhadap kadar glukosa tikus Wistar (*Rattus norvegicus*) yang diindikasi aloksan. Jurnal e-Biomedik 3(1):1–6

Cantley J, Ashcroft FM (2015) Q&a: insulin secretion and type 2 diabetes: why do β-cells fail? BMC Biol 13(13):1–7

Cao H, Graves DJ, Anderson RA (2010) Cinnamon extract regulates glucose transporter and insulin-signaling gene expression in mouse adipocytes. Phytomedicine 17(13):1027–1032

Chauhan V, Kashyap D, Chauhan N (2020) Alpha-amylase inhibition assay and qualitative analysis of aqueous foliar extract of *Piper betle*. World J Pharm Res 10(3):1564–1571

Delfita R, Tjong DH, Dahelmi D, Suhatri S (2020) Hypoglycemic effects of Enhydra fluctuans aerial extract on alloxan-induced diabetic rats, translated by Padang. IOP Publishing Ltd., Indonesia, p 012058

Denta AO, Watiningrum RY, Susilawati EF (2022) Serbuk daun kelor efektif menurunkan kadar glukosa darah dan kadar kolesterol pada individu obese. Wiraraja Medika: Jurnal Kesehatan 12(1):10–16

Deviana KZ, Diniatik D (2021) Analisis penambatan molekuler dan prediksi toksisitas dan ADME penghambat enzim dipeptidil peptidase IV dari senyawa aktif *Momordica charantia* L. sebagai antidiabetes. PHARMACY: Jurnal Farmasi Indonesia (Pharm J Indonesia) 18(2):361–370

Dewijanti ID, Mangunwardoyo W, Artanti N, Hanafi M (2019) Bioactivities of Salam leaf (*Syzygium polyanthum* (Wight) Walp). AIP Conf Proc 2168:020072

Divi SM, Bellamkonda R, Dasireddy SK (2012) Evaluation of antidiabetic and antihyperlipedemic potential of aqueous extract of *Moringa oleifera* in fructose fed insulin resistant and STZ induced diabetic wistar rats: a comparative study. Asian J Pharm Clin Res 5:67–72

Emelda A, Rahman S and Rahmah AS (2015) Uji efek hipoglikemik infus daun mangga varietas golek terhadap mencit (Mus musculus) diabetik yang telah diinduksi aloksan, 1.

Farkhani A, Sauriasari R, Yanuar A (2020) *In silico* approach for screening of the Indonesian medicinal plants database to discover potential dipeptidyl peptidase-4 inhibitors. Int J Appl Pharm 12(1):60–68

Fatmalia N (2017) Pengaruh konsumsi Kayu Manis terhadap glukosa darah penderita diabetes mellitus di Tambak Ploso Lamongan. J Ners Commun 08(1):106–111

Fikriyah M, Almurdani M, Eryanti Y, Teruna HY (2020) Antidiabetic activity of triterpenoids from *Anisophyllea disticha*. J Phys Conf Ser 1655(1):012033

Firdaus MD, Artanti N, Hanafi M (2021) Phytochemical constituents and *in vitro* antidiabetic and antioxidant properties of various extracts of Kenikir (*Cosmos caudatus*) leaves. Pharmacogn J 13(4):890–895

Ghosh D, De D, Chatterjee K, Ali KM, Bera TK (2011) Antidiabetic potentiality of the aqueous-methanolic extract of seed of *Swietenia mahagoni* (L.) Jacq. in streptozotocin-induced diabetic male albino rat: a correlative and evidence-based approach with antioxidative and antihyperlipidemic activities. Evid-Based Compl Alternat Med 2011:1–11

Gina LP, Mahdi C, Aulanni'am, (2014) The influence water extract of black soybean (*Glycine max* (L.) Merr) on reducing of blood glucose level and the superoxide dismutase (SOD) activity on diabetes mellitus rats induced with multiple low dose of streptozotocin (MLD-STZ). J Pure Appl Chem Res 3(3):131–137

Gunawan-Puteri MD, Kato E, Kawabata J (2012) Alpha-amylase inhibitors from an Indonesian medicinal herb, *Phyllanthus urinaria*. J Sci Food Agric 92(3):606–609

Gupta R, Mathur M, Bajaj VK, Katariya P, Yadav S, Kamal R, Gupta RS (2012) Evaluation of antidiabetic and antioxidant activity of *Moringa oleifera* in experimental diabetes. J Diabetes 4(2):164–171

Hajra S, Mehta A, Pandey P, Vyas S (2011) Antioxidant and antidiabetic potential of ethanolic extract of *Swietenia mahagoni* (Linn.) seeds. Int J Pharmaceut Res Dev 3:180–186

Hassan Z, Yam MF, Ahmad M, Yusof APM (2010) Antidiabetic properties and mechanism of action of *Gynura procumbens* water extract in streptozotocin-induced diabetic rats. Molecules 15:9008–9023

Hayati F, Chabib L, Sekarraras FD, Faizah WS (2021) Antihyperglycemic activity of *Centella asiatica* (L.) Urb. leaf ethanol extract SNEDDS in zebrafish (*Danio rerio*). Open Chem 19(1):184–188

Hefti FF (2008) Requirements for a lead compound to become a clinical candidate. BMC Neurosci 9(3):1–7

IDF (2021) IDF Diabetes Atlas, 10th ed.

Indonesia, B. P. O. d. M. R. (2022) Peraturan Badan Pengawas Obat dan Makanan No. 31 Tahun 2022, Jakarta: Badan Pengawas Obat dan Makanan

Indonesia KKR (2010) Peraturan Menteri Kesehatan Republik Indonesia No: 003/MENKES/PER/2010. Kementerian Kesehatan Republik Indonesia, Jakarta

Indonesia, K. K. R. (2021a) 'Fitofarmaka berpotensi jadi produk farmasi utama dalam negeri', [online], available: https://sehatnegeriku.kemkes.go.id/baca/umum/20211108/5038813/fitofarmaka-berpotensi-jadi-produk-farmasi-utama-dalam-negeri/ [Accessed 27 September 2023]

Indonesia, K. K. R. (2021b) 'Forum Nasional Kemandirian Industri Sediaan Farmasi', [online], available: https://farmalkes.kemkes.go.id/2021/11/forum-nasional-kemandirian-industri-sediaan-farmasi/ [Accessed 2023].

Indonesia KPR (2015) 'Bahan baku obat di Indonesia 90% masih impor', [online], available: https://kemenperin.go.id/artikel/12156/Bahan-Baku-Obat-di-Indonesia-90-Masih-Impor [Accessed 27 September 2023 2023].

Indonesia, K. R. T. d. P. T. R. (2019) Peraturan Menteri Riset, Teknologi, Dan Pendidikan Tinggi Republik Indonesia Nomor 38 Tahun 2019 tentang Prioritas Riset Nasional Tahun 2020–2024,

Ioannidis JPA (2012) Extrapolating from animals to humans. Sci Transl Med 4(151):151ps15-151ps15

Irawan C, Sukiman M, Ismail I, Putri ID, Utami A, Pratama AN, Kumala Zalni MI (2022) Antioxidant capacity and potential as an alpha-glucosidase inhibitor in *Phaleria macrocarpa* (Scheff.) Boerl fruit peel ultrasonic extract. Pharm J 14(4):305–312

Jafar N, Qalbi FN, Thaha RM, Hadju V, Hidayanti H, Salam A, Syam A (2020) Effect of *Cinnamomum burmannii* stew on glucose fasting blood levels in adult prediabetes in Makassar. Open Access Maced J Med Sci 8(T2):71–74

Jati Pramono V, Santoso R (2014) Pengaruh Ekstrak Buah Kersen (Muntingia calabura) Terhadap Kadar Gula Darah Tikus Putih (Rattus novergicus) yang Diinduksi Streptozotocin (STZ) Effect Of Keren Fruit Extract (Muntingia calabura) On Blood Glucose Levels Of Rats (Rattus novergicus) Which Induced. Jurnal Sains Veteriner 32(2):218–223

Kadota S, Marpaung L, Kikuchi T, Ekimoto H (1990) Constituents of the *Swietenia mahagoni* Jacq. Isolation, structures and ^{1}H and ^{13}C-nuclear magnetic resonance signal assignments of new tetranortriterpenoids related to Swietenine, and Swietenolide. Chem Pharm Bull 38(3):639–651

Kalaivanan K, Pugalendi KV (2011) Antihyperglycemic effect of the alcoholic seed extract of *Swietenia macrophylla* on streptozotocin-diabetic rats. Pharmacogn Res 3(1):67–71

Kamalakkannan N, Prince PSM (2006) Antihyperglycaemic and antioxidant effect of rutin, a polyphenolic flavonoid, in streptozotocin-induced diabetic wistar rats. Basic Clin Pharmacol Toxicol 98(1):97–103

Kurniawati D, Jasaputra DK, Dewi K, Sujatno M, Putra MS, Sallyvania MY, Juanda IJ (2010) Effect of *Physalis minina* Linn, *Psidium guajava* Linn., *Sweitenia mahagoni* Jacq ethanol extract against blood glucose level. J Medika Planta 1(2):55–60

Larantukan SVM, Setiasih NLES, Widyastuti SK (2014) Pemberian ekstrak etanol kulit batang Kelor glukosa darah tikus hiperglikemia. Indonesia Medicus Veterinus 3(4):292–299

Li D-D, Chen J-H, Chen Q, Li G-W, Chen J, Yue J-M, Chen M-L, Wang X-P, Shen J-H, Shen X, Jiang H-L (2005)

Swietenia mahagony extract shows agonistic activity to PPARγ and gives ameliorative effects on diabetic db/db mice. Acta Pharmacol Sin 26(2):220–222

Lolok N, Ramadhan DSF, Sumiwi SA, Sahidin I, Levita J (2022) Molecular docking of *β*-sitosterol and stigmasterol isolated from *Morinda citrifolia* with α-amylase, α-glucosidase, dipeptidylpeptidase-IV, and peroxisome proliferator-activated receptor-γ. Rasayan J Chem 15(1):20–30

Mahid-Al-Hasan S, Khan MI, Umar BU (2015) Effect of ethanolic extract of *Swietenia mahagoni* seeds on experimentally induced diabetes mellitus in rats. Faridpur Med Coll J 6(2):70–73

Makanan, B. P. O. d. (2023) 'Monitoring dan evaluasi pendampingan UMKM obat tradisional oleh fasilitator UPT BPOM', [online], available: https://pmpuotskkos.pom.go.id/view/more/news/27014 [Accessed 1 Oktober 2023].

Malik A, Ahmad AR (2016) Antidiabetic effect of standardized extract of Indonesian Kanunang leaves (*Cordia myxa* L.). Int J PharmTech Res 9(8):268–275

Mangallo B, Putra ABP, Pulung ML (2019) Uji aktivitas antidiabetes dengan metode penghambatan enzim α-Glukosidase dan karakterisasi kandungan senyawa aktif pada fraksi metanol dan kloroform daun Lavetar (*Wedelia biflora* (L). DC) asal biak. J Nat 15(1):21–29

Mardiansyah RA (2020) Pengaruh efek ekstrak Sambiloto terhadap penurunan kadar glukosa darah tikus putih yang diinduksi streptozotocin. Jurnal Medika Hutama 2(1):287–291

Mbikay M (2012) Therapeutic potential of *Moringa oleifera l*eaves in chronic hyperglycemia and dyslipidemia: a review. Front Pharmacol 3:1–12

Meneses MJ, Silva BM, Sousa M, Sá R, Oliveira PF, Alves MG, Alves MG (2015) Antidiabetic drugs: mechanisms of action and potential outcomes on cellular metabolism. Curr Pharm des 21(25):3606–3620

Millati A, Bahar Y, Kusumawinakhyu T (2019) Pengaruh sediaan dekok daun Zaitun (*Olea europaea* L.) terhadap kadar glukosa darah pada tikus putih galur Wistar (*Rattus norvegicus*) galur Wistar jantan. Her-Med J 2(2):20–26

Muhammad A, Maria B, Suryani, Mega S, Waras N (2020) Kinetics of α -glucosidase inhibitory activity and phytochemical analysis of Piper crocatum Ruiz & Pav leaves ethanol extract. Int J Res Pharm Sci 11(4):2032–2036

Munawwarah ZF, Wahid RAH, Marfu'ah N (2019) Uji Efektivitas Seduhan Kopi Biji Okra (*Abelmoschus esculentus*) terhadap penurunan kadar glukosa darah pada mencit yang diinduksi Aloksan. Pharm J Islamic Pharm 3(2):1–9

Kasolo JN, Bimenya GS, Ojok L, Ochieng J, Ogwal-Okeng JW (2010) Phytochemicals and uses of *Moringa oleifera* leaves in Ugandan rural communities. J Med Plants Res 4(9):753–757

Naeem S, Hylands P, Barlow D (2012) Construction of an Indonesian herbal constituents database and its use in random forest modelling in a search for inhibitors of aldose reductase. Bioorg Med Chem 20(3):1251–1258

Namazi N, Khodamoradi K, Khamechi SP, Heshmati J, Ayati MH, Larijani B (2019) The impact of cinnamon on anthropometric indices and glycemic status in patients with type 2 diabetes: a systematic review and meta-analysis of clinical trials. Complement Ther Med 43:92–101

Nipun TS, Khatib A, Ibrahim Z, Ahmed QU, Redzwan IE, Primaharinastiti R, Saiman MZ, Fairuza R, Widyaningsih TD, AlAjmi MF, Khalifa SAM, El-Seedi HR (2021) GC-MS- and NMR-based metabolomics and molecular docking reveal the potential *alpha*-glucosidase inhibitors from *Psychotria malayana* Jack leaves. Pharmaceuticals 14(10):978

Nisar B, Sultan A, Rubab SL (2017) Natural products chemistry & comparison of medicinally important natural products versus synthetic. Nat Products Chem Res 6(2):1–2

Nurdin SU, Sukohar A (2017) Antiglucosidase and antioxidant activities of Ginger, Cinnamon, Turmeric and their combination. Int J Pharm Pharm Res 10(1):296–306

O'Rourke A, Beyhan S, Choi Y, Morales P, Chan AP, Espinoza JL, Dupont CL, Meyer KJ, Spoering A, Lewis K, Nierman WC, Nelson KE (2020) Mechanism-of-action classification of antibiotics by global transcriptome profiling. Antimicrob Agents Chemother 64(3):e01207-e1219

Ota H, Akishita M, Tani H, Tatefuji T, Ogawa S, Iijima K, Eto M, Shirasawa T, Ouchi Y (2013) Trans-resveratrol in *Gnetum gnemon* protects against oxidative-stress-induced endothelial senescence. J Nat Prod 76(7):1242–1247

Panggabean FK, Triastuti E, Yunita EP (2014) Uji aktivitas peningkatan sensitivitas insulin ekstrak biji Jintan Hitam (*Nigella sativa*) melalui pengukuran konsentrasi tirosin terfosforilasi insulin reseptor substrat. Majalah Kesehatan 1(1):53–59

Prakoso LBA, Mambo C and Wowor MP (2016) 'Uji efek ekstrak buah okra (*Abelmoschus esculentus*) terhadap kadar glukosa darah pada tikus wistar (*Rattus norvegicus*) yang diinduksi aloksan', *Jurnal e-Biomedik,* 4(2):1-5

Purnamasari AB, Rusdianto (2021) 'Effect of brotowali extract fortification of papaya leaves and sugar cane caries on Diabetes Mellitus Type II. J Phys: Conf Series 1752:012051

Putri DA, Fatmawati S (2019) A new flavanone as a potent antioxidant isolated from *Chromolaena odorata* L. leaves. Evid Based Complement Alternat Med 2019:1453612

Putri NSY, Islami D, Tresna AT, Hidayah LN, Mubarakati NJ, Jayanti GE (2022) *Molecular docking atudy of Takokak plants (Solanum torvum) to α-glucosidase as antidiabetic Type-2,* translated by Tarakan. University Of Borneo, Indonesia, pp 1–7

Rachid AP, Moncada M, de Mesquita MF, Brito J, Silva ML, Bernardo MA (2022) Effect of aqueous cinnamon extract on the postprandial glycemia levels in patients with type 2 Diabetes Mellitus: a randomized controlled trial. Nutrients. https://doi.org/10.3390/nu14081576

Rahmah F, Febriani H, Rasyidah, (2021) 'Uji efektivitas ekstrak etanol Bawang Batak (*Allium chinense* G. Don.) terhadap histopatologi hati tikus putih (*Rattus* norvegicus L.) Diabetes Melitus. BEST J (Biol Educ Sains Technol 4(2):07–13

Rani DM, Hanafi N, Rachmawati D, Siswoyo TA, Christianty FM, Dewi IP, Nugraha AS (2023) Indonesian vegetables: searching for antioxidant and antidiabetic therapeutic agents. Drugs Drug Candid 2(1):14–36

Ratnadewi AAI, Wahyudi LD, Rochman J, Nugraha Susilowati AS, Siswoyo TA (2020) 'Revealing antidiabetic potency of medicinal plants of Meru Betiri National Park, Jember – Indonesia. Arab J Chem 13(1):1831–183

RI, K. K. (2021) 'Fitofarmaka berpotensi jadi produk farmasi utama dalam negeri', [online], available: https://sehatnegeriku.kemkes.go.id/baca/umum/20211108/5038813/fitofarmaka-berpotensi-jadi-produk-farmasi-utama-dalam-negeri/ [Accessed 24 Januari 2022 2022].

Riyanti S, Suganda AG, Sukandar EY (2016) Dipeptidyl peptidase-IV inhibitory activity of some Indonesian medicinal plants. Asian J Pharm Clin Res 9(2):375–377

Roberts CK, Havener AL, Barnard RJ (2013) Metabolic syndrome and insulin resistance: underlying causes and modification by exercise training. Compr Physiol 3(1):1–58

Rockwood JL, Anderson BG, Casamatta DA (2013) Potential uses of *Moringa oleifera* and an examination of antibiotic efficacy conferred by *M. oleifera* seed and leaf extracts using crude extraction techniques available to underserved indigenous populations. Int J Phytother Res 3(2):61–71

Rohman F, Putra WE, Sustiprijatno and Widiastuti, D. (2021) 'Virtual assessment of *Imperata cylindrica* root′s bioactive compounds as a potential inhibitor for alpha-glucosidase: the study of Tengger tribe′s medicinal plant. Tropical J Nat Product Res 5(7):1240–1245

Safithri M, Fahma F (2008) Potency of *Piper crocatum* decoction as an antihiperglycemia in rat atrain *Sprague dawley*. HAYATI J Biosci 15(1):45–48

Sahgal G, Ramanathan S, Sasidharan M, Ismail and Mansor (2009) Phytochemical and antimicrobial activity of *Swietenia mahagoni* crude methanolic seed extract. Tropical Biomed 26(3):274–279

Sarbunan TL, Datu OS, Maarisit W, Untu SD, Kanter JW (2021) Uji efek pemberian ekstrak etanol kulit buah Sirsak (*Annona muricata* Linn.) sebagai antidiabetes pada tikus putih (*Rattus norvegicus*) yang diinduksi. Jurnal Biofarmasetikal Tropis 4(2):39–43

Sari BL, Mun'im A, Yanuar A, Riadhi R (2016) Screening of α-glucosidase inhibitors from *Terminalia catappa* L. fruits using molecular docking method and *in vitro* test. Int J Pharm Pharm Sci 8(12):184

Setiawansyah A, Reynaldi M, Tjahjono DH, Sukrasno S (2022) Molecular docking-based virtual screening of antidiabetic agents from Songga (*Strychnos lucida* R.Br.): an Indonesian native plant. Curr Res Biosci Biotechnol 3:208–214

Shimada T, Kato F, Dwijayanti DR, Nagata T, Kinoshita A, Okuyama T, Nishizawa M, Mukai E (2022) Bitter melon fruit extract enhances intracellular ATP production and insulin secretion from rat pancreatic β-cells. Br J Nutr 127(3):377–383

Siahaan JM, Illyas S, Lindarto D, Nainggolan M (2021) The effect of ethanol extract and ethyl acetic fraction of standardised chayote squash to reduce blood sugar level and the function of pancreatic β-cell of male albino rats induced by STZ-NA-HFD. Rasayan J Chem 14(1):65–73

Simorangkir M, Sinaga E, Silaban S (2022) Hepatoprotective and histological pancreas effects of Sarang Banua (*Clerodenrum fragrans* Vent Willd) leaf extract in alloxan-induced diabetic rats. Rasayan J Chem 15(3):1846–1854

Sinulingga S, Haryadi K, Pradika Y (2018) Efficacy of *Morinda citrifolia* fruit extract to increase insulin synthesis in wistar rats-induced diabetics. Res J Pharm Biol Chem Sci 9(5):1558–1562

Sinurat MR, Rahmayanti Y, Rizarullah R (2021) Uji aktivitas antidiabetes senyawa baru daun Yakon (*Smallanthus sonchifolius*) sebagai inhibitor enzim DPP-4: Studi *in silico*. Jurnal IPA Dan Pembelajaran IPA 5(2):138–150

Sukardiman and Ervina M (2020) The recent use of *Swietenia mahagoni* (L.) Jacq. as antidiabetes type 2 phytomedicine: a systematic review. Heliyon 6(3):e03536

Sukardiman PN, Studiawan H, Arifianti L (2017) Antidiabetic activity of dry extracts of *Swietenia mahagoni* seeds in alloxan-induced diabetic Balb/C. World J Pharmaceut Res 6:1334–1339

Suri MA, Azizah Z, Asra R (2021) Traditional use, phytochemical and pharmacological review of red betel leaves (*Piper crocatum* Ruiz & Pav). Asian J Pharm Res Dev 9(1):159–163

Suryani N, Endang TH, Aulanni'am, (2013) Pengaruh ekstrak metanol biji mahoni terhadap peningkatan kadar insulin, penurunan ekspresi TNF-α dan perbaikan jaringan pankreas tikus diabetes. Jurnal Kedokteran Brawijaya 27(3):137–145

Sutrisna EM, Hervian L, Sahadewa FA (2018) Hypoglicemic effect of 70% ethanolic extract of *Tinospora crispa* L. (Bratawali) stem from indonesia in wistar rat induced by alloxan. J Clin Diagnos Res 12(9):FF01

Sutrisna EM, Hervian L, Sahadewa FA (2018) Hypoglicemic effect of 70% ethanolic extract of Tinosporacrispa L. (Bratawali) stem from indonesia in wistar rat induced by alloxan. J Clin Diagn Res 12(9):FF01

Syabana MA, Yuliana ND, Batubara I, Fardiaz D (2022) Alpha-glucosidase inhibitors from *Syzygium polyanthum* (Wight) Walp leaves as revealed by metabolomics and in silico approaches. J Ethnopharmacol 282:114618

Syamra A, Indrawati A, Warsyidah AA (2018) Pemberian rebusan daun Kelor terhadap penurunkan kadar glukosa darah pada pasien penderita Diabetes Mellitus (DM). J Med Lab 8:50–55

Tamarai K, Bhatti JS, Reddy PH (2019) Molecular and cellular bases of diabetes: focus on type 2 diabetes mouse model-TallyHo. Biochimica Et Biophysica Acta (BBA)—Mol Basis Disease 1865(9):2276–2284

Tandrasasmita OM, Wulan DW, Sinambela J, Tjandrawinata RR, Nailufar F (2011) Glucose-lowering effect of DLBS3233 is mediated through phosphorylation of tyrosine and upregulation of PPARg and GLUT4 expression. Int J General Med 4:345–345

Taylor R (2012) Insulin resistance and type 2 diabetes. Diabetes 61(4):778–779

Tjokroprawiro A, Murtiwi S, Tjandrawinata RR (2016) DLBS3233, a combined bioactive fraction of *Cinnamomum burmanii* and *Lagerstroemia speciosa*, in type-2 diabetes mellitus patients inadequately controlled by metformin and other oral antidiabetic agents. J Complement Integr Med 13(4):413–420

Venkatachalam T, Kumar VK, Selvi PK, Maske AO, Anbarasan V, Kumar PS (2011) Antidiabetic activity of *Lantana camara* Linn fruits in normal and streptozotocin-induced diabetic rats. J Pharm Res 4(5):1550–1552

Wahyuni T (2021) Potensi antioksidan ekstrak etanol daun Belimbing (*Averrhoa bilimbi* L.) dan pengaruhnya terhadapa kadar darah pada tikus Wistar jantan yang diinduksi Streptozotosin. Indonesian Pharm Nat Med J 5(1):9–9

WHO (2023) 'Diabetes', [online], available: https://www.who.int/news-room/fact-sheets/detail/diabetes [Accessed 19 June 2024 2024].

Widiyanto A, Anwar E, Nurhayati T (2018) In vitro assay of *a*-glucosidase inhibitor activities of three aeagrasses from Banten bay, Indonesia. Pharmacogn J 10(5):907–910

Widiyono and Suwarni A (2019) Rebusan daun Sirih Merah berpengaruh pada penurunan glukosa darah penderita Diabetes Mellitus tipe II. Jurnal Ilmu Keperawatan 12(2):140–149

Widjaja SS, Munir D, Rusdiana, Savira M (2017) Extract ethanol of poguntano as anti diabetic in alloxan induced diabetic rats. Int J ChemTech Res 10(2):103–107

Widyawati T, Pane YS, Yusoff NA (2019) Effect of *Lawsonia inermis* Linn. extracts on blood glucose level in normal and streptozotocin-induced diabetic rats. Pak J Nutr 18(7):671–676

Widyawati T, Yusoff NA, Asmawi MZ, Ahmad M (2015) Antihyperglycemic effect of methanol extract of *Syzygium polyanthum* (Wight.) leaf in streptozotocin-induced diabetic rats. Nutrients 7(9):7764–7780

Wresdiyati T, Sa'Diah S, Winarto ADI, Febriyani V (2015) *a*-glucosidase inhibition and hypoglycemic activities of *Sweitenia mahagoni* seed extract. HAYATI J Biosci 22(2):73–78

Wu H-S, Zhu D-F, Zhou C-X, Feng C-R, Lou Y-J, Yang B, He Q-J (2009) Insulin sensitizing activity of ethyl acetate fraction of *Acorus calamus* L. *in vitro* and *in vivo*. J Ethnopharmacol 123(2):288–292

Yazid F, Salim S, Rahmadika F, Artanti N, Sundowo A, Prasasty V, Sofyan R (2021a) Antidiabetic effects of *Tithonia diversifolia* and *Malus domestica* leaf extracts in Alloxan-induced *Sprague Dawley* rats. Syst Rev Pharm 12(1):1630–1638

Yazid F, Salim SO, Rahmadika FD, Rosmalena R, Artanti N, Sundowo A, Prasasty VD (2021b) Antidiabetic effects of *Tithonia diversifolia* and *Malus domestica* leaf extracts in alloxan-induced sprague dawley rats. Syst Rev Pharm 12(1):1630–1638

Yonemoto R, Shimada M, Gunawan-Puteri MD, Kato E, Kawabata J (2014) A-amylase inhibitory triterpene from *Abrus precatorius* leaves. J Agric Food Chem 62(33):8411–8414

Yp N, Urooj A (2015) Amelioration of diabetes by *Swietenia mahagoni* in streptozotocin induced diabetic rats. Int J Pharm Sci Res 6(9):3892–3892

Zolkeflee NKZ, Ramli NS, Azlan A, Abas F (2022) *In vitro* antidiabetic activities and UHPLC-ESI-MS/MS profile of *Muntingia calabura* leaves extract. Molecules 27(1):1–21