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Australian tropical medicinal plants and their phytochemicals with wound healing and antidiabetic properties

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Abstract Diabetes remains a global health challenge, with increasing numbers of patients diagnosed annually. Managing diabetes, particularly type two diabetes (T2D), requires a healthy lifestyle and medication to prevent further complications. New and effective antidiabetic drugs derived from natural products, including medicinal plants, are urgently needed because of the undesirable side effects associated with current antidiabetic drugs. Australian Aboriginal people possess rich traditional knowledge of plants used for food and therapeutic purposes. Here, we reviewed the literature on Aboriginal medicinal plants and found that a total of 126 Australian tropical plant species belonging to 47 families and 88 genera were reported as being used for treating wounds and diabetes-related conditions. We found that 28 of these 126 species were edible, of which fruits were the most consumed part. Among the 126 species, crude extracts from 29 species have been tested for their antidiabetic properties, and crude extracts of *Syzygium cumini* and *Morinda citrifolia* were the most extensively studied. Crude extracts from some species (e.g., *Morinda citrifolia*, *Eleocharis dulcis,* and *Brassica rapa*) have also been clinically evaluated in diabetic patients. Additionally, among 29 species, 374 pure compounds were isolated from 26 species. From the 374 isolated compounds, 51 have already been tested, out of which 16 were identified as antidiabetic drug leads. A total of 73 Aboriginal medicinal plants have not been tested for their phytochemical content or antidiabetic activity. These plants not only present potential targets for the biodiscovery of novel antidiabetic drug leads but also for the development of antidiabetic nutraceuticals based on traditional bush food knowledge.

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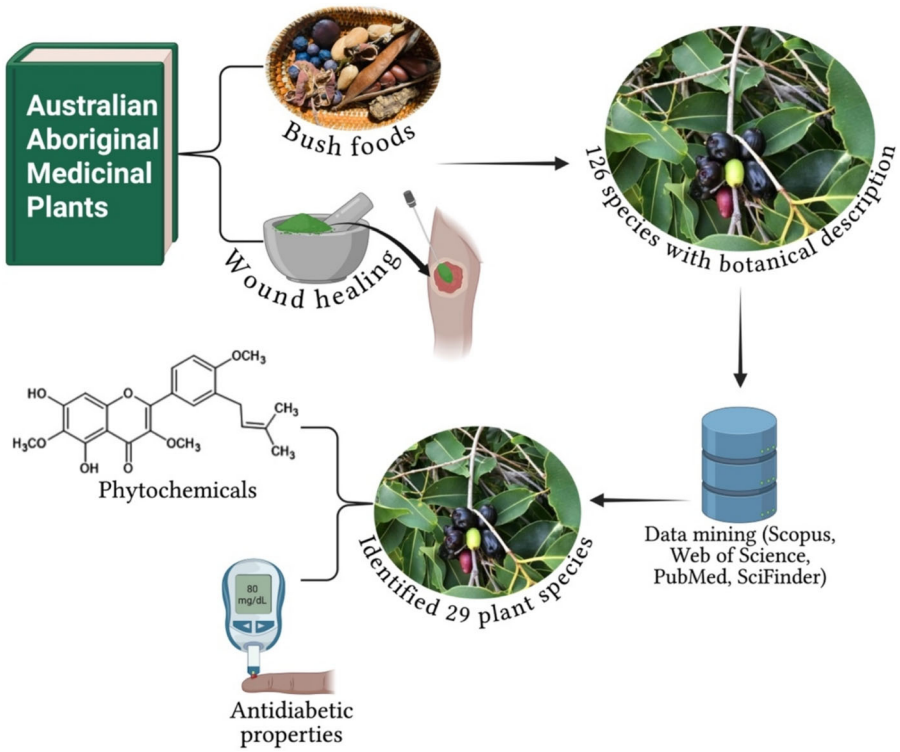
Graphical abstract



Keywords Aboriginal people · Antidiabetic activity · Diabetes · Medicinal plants · Phytochemicals · Wound healing

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Introduction

Diabetes is a chronic metabolic disorder characterised by hyperglycemia, which may lead to damage to various organs, including the kidneys, nerves, eyes, heart, and blood vessels (WHO 2024). Diabetes is diagnosed as either type 1 or type 2 diabetes (T2D). Type 1 diabetes (T1D) occurs because of a complete lack of insulin, which occurs when pancreatic beta cells are destroyed. This destruction is due to genetic factors influenced by viral infections and autoimmune diseases (Ikegami et al. 2021). T1D is characterised by hyperglycemic conditions and weight loss because of increased lipolysis and protein breakdown. This type typically occurs in young people and requires insulin supplements (Ikegami et al. 2021; Lega and Lipscombe 2020). On the other hand, T2D mainly occurs in overweight people who develop insulin resistance or relative insulin deficiency (WHO 2024; Galicia-Garcia et al. 2020). Insulin insensitivity is triggered by obesity due to genetic disposition and an imbalance in energy uptake and expenditure, which increase the

fatty acid concentration in the blood. This condition reduces glucose utilisation in muscle and fatty tissues, resulting in insulin resistance and increased insulin secretion (Silbernagl et al. 2016; Jameson 2010).

The International Diabetes Federation (IDF) reported that approximately 537 million adults aged 20–79 years were diagnosed with severe diabetes in 2021 (IDF 2021), 90% of whom had T2D (Henning 2018; WHO 2024). On the basis of the current incidence rate, the number of diabetes cases is projected to increase to 643 million by 2030 and 783 million by 2045, with the highest prevalence in low- to middle-income countries, which are projected to constitute 3 in 4 adults with diabetes (IDF 2021). China and India are the top countries, with 140.9 and 74.2 million people with diabetes, respectively, in 2021 (Sun et al. 2022; IDF 2021). In Australia, 1.4 million people were living with diabetes in 2021 (AIHW 2024). The high prevalence of T2D is driven mainly by physical inactivity and energy-dense diets, leading to obesity and an aging population (WHO 2024; Chatterjee et al. 2017). These conditions cause hyperglycemia and insulin resistance, leading to diabetes complications such as cardiovascular diseases (Ali et al. 2022; Galicia-Garcia et al. 2020). In 2023, T2D was responsible for approximately 124,000 years of healthy life lost and contributed 2.2% to the total disease burden in Australia, and it was the 11th leading cause of disease burden (AIHW 2024). Diabetes is not only a global health problem but also a major economic burden. The global cost of diabetes in 2021 was estimated to be US$966 billion (11.5% of the global health expenditure) (IDF 2021). For example, Australia's healthcare and productivity losses associated with managing T2D (along with cardiovascular diseases) are estimated to be AU$ 421.15 and AU$ 577.04 billion, respectively, between 2020 and 2030 (Abushanab et al. 2022; Henning 2018).

There is still no cure for T2D, and it can be managed only through a healthy lifestyle, diet, and medication with various antidiabetic drugs (WHO 2024; Tan et al. 2019). Most currently available antidiabetic drugs, including metformin (the frontline drug for T2D), help regulate blood glucose concentration/level (glycaemic control) by triggering more insulin release from the pancreas and increasing urinary glucose excretion (Tan et al. 2019; Scheen 2020; Wilson 2010). Despite their therapeutic benefits, most antidiabetic drugs have side effects (Ali et al. 2022; Xu et al. 2018). For example, metformin can effectively lower blood glucose concentrations, but it is linked to vitamin B12 deficiency and is not recommended for patients with moderate to severe chronic kidney disease (Chatterjee et al. 2017; Tan et al. 2019). Sodium-glucose cotransporter 2 (SGLT2) inhibitor drugs are implicated in diabetic ketosis, kidney problems, and urinary tract and genital infections (Mashraqi et al. 2021). Glucagon-like peptide-1 (GLP-1) receptor agonist drugs cause gastrointestinal effects such as nausea, vomiting, diarrhoea, and constipation (Wharton et al. 2022). Thus, there is a strong demand for new and safer antidiabetic drugs (Jugran et al. 2021; Ali et al. 2015).

Antidiabetic compounds from plants often show greater efficacy with fewer side effects than synthetic drugs do (Wasana et al. 2021; Arulselvan et al. 2014), and most of these compounds have been isolated on the basis of traditional knowledge. Plant-based formulations (derived from traditional medicine knowledge) have long been used to manage diabetes and diabetes-related conditions. Australian Aboriginal people have used plants for food and therapeutic purposes for thousands of years, accumulating vast knowledge of the properties of these plants (Cribb and Cribb 1981; Barr et al. 1993). Aboriginal people have been called "food gatherers" because of their ability to sustain themselves and acquire the most intricate skills to meet the challenges of nature (Low 1989). Many plants are used to treat diabetes-related conditions, such as cuts, sores, boils, burns (DiabetesAustralia 2024), and digestive disorders (Mapp 1986), with decoctions, ointments, and infusions prepared from different parts of the plants (Clarke 2007; Williams 2010). In addition, indigenous people are aware of variations in the active components associated with soil type (Lassak and McCarthy 2011). Given that impaired wound healing is one of the major complications associated with diabetes (Chen et al. 2024; Stachura et al. 2022; Dubey et al. 2022), we hypothesised that the Aboriginal medicinal plants used to treat wounds or cuts could be potential sources of antidiabetic drug leads.

Therefore, the main aim of this review was to evaluate the antidiabetic or wound-healing properties, or efficacy of crude extracts, fractions, and isolated pure compounds reported from Aboriginal tropical medicinal plants in Australia. This review also aimed

to compile phytochemical and antidiabetic activity profiles of those medicinal plants that have already been studied as a knowledge database to support the traditional use of Aboriginal medicinal plants.

Literature review method

Figure 1 presents an overview of the strategy applied in this review. Initially, data for 149 plant species were retrieved from various books on Aboriginal medicinal plants, bush foods, and bush medicines across Australia (Cribb and Cribb 1981; Barr et al. 1993; Low 1989, 1990; Clarke 2007; Kyriaziz 1995; Williams 2010; Lassak and McCarthy 2011; Bindon 1996; Maiden 1889; Edgar et al. 1997; Webb 1959). These 149 medicinal plants were used by Australian Aboriginal people to treat diabetes-related conditions. Five datasets were further examined, namely, the Atlas of Living Australia (ALA) for plant descriptions (ALA 2024), the Australasian Virtual Herbarium (AVH) for plant distributions (AVH 2024), the World Flora Online (WFO) Plant (WFO 2024) and the Australian Plant Census (APC) for taxonomy (APC 2024), and the Useful Tropical Plants (UTP) database (UTP 2024) for additional information, including habits, parts used, and ethnomedicinal uses. The following hits were excluded: poisonous plants (5 species), plants outside the Australian Tropical Regions (5 species), and data that were not incorporated under the current plant name (13 species). The 126 species were further reviewed via online databases, such as Scopus, PubMed, Web of Science, and SciFinder, which use plant names and relevant keywords such as 'antidiabetic,' 'diabetes,' 'isolated compounds,' 'crude extract,' and 'antidiabetic compounds.'

Results and discussion

Traditional wound-healing medicinal plants with antidiabetic potential

The Aboriginal tropical medicinal plants reviewed here were chosen for their traditional use in wound healing, as terms like 'hyperglycemia' were not used in ancient times. Today, it is well established that glucose metabolism is essential for wound healing, providing the energy required for cellular and tissue repair (Demling 2009; Eming et al. 2021; Im and Hoopes 1970). However, in diabetic patients, impaired glucose regulation leads to chronic wounds and delayed healing (Patel et al. 2019). This disruption in normal wound repair process is driven by factors such as persistent hyperglycemia, nerve damage, and vascular complications, which can result in infections, ulcers, and even limb amputation (Falanga 2005; Brem and Tomic-Canic 2007).

Modern therapeutic strategies for diabetes, including dipeptidyl peptidase-4 (DPP-4) inhibitors and metformin, have shown promise in supporting wound healing (Spampinato et al. 2020; Han et al. 2017). Additionally, natural compounds like betulinic acid have been found to accelerate diabetic wound healing by reducing inflammation and oxidative stress (Yadav et al. 2024). These findings highlight a significant link between the wound healing effects of medicinal plants and their antidiabetic properties (Oguntibeju 2019). Several medicinal plants traditionally used for wound healing have also exhibited antidiabetic effects, suggesting a valuable dual therapeutic potential. For instance, *Aloe vera* leaf has been widely applied in traditional medicine for treating burns and skin injuries, and studies have confirmed its role in glycemic control and improving insulin sensitivity in diabetic models (Adamu et al. 2021). *Azadirachta indica* (commonly known as neem) is another example. It is commonly used for its antimicrobial and wound-healing properties, and also shown to exert hypoglycemic effects in both animal and clinical studies (Rafe 2017). Similarly, seeds of *Trigonella foenum-graecum* (Fenugreek), traditionally used in wound poultices, have demonstrated antidiabetic activity through delayed glucose absorption and improved insulin function (Bharathy and Thanikachalam 2024).

Australian tropical medicinal plants with antidiabetic properties

In Australia, more than 500 species of native plants have been documented for their medicinal uses, highlighting the country's rich biodiversity and the rich traditional biocultural knowledge held by indigenous communities (Cribb and Cribb 1981). Many of these plants have been used to treat a range of ailments, including metabolic disorders. Our review led to the identification of 126 medicinal plants (Fig. 1) that are traditionally used by Aboriginal people to treat

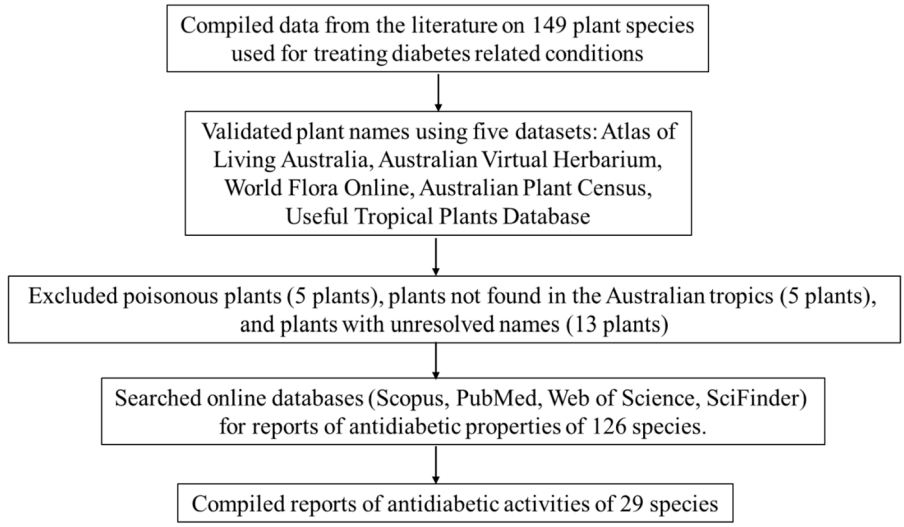

Fig. 1 Overview of strategies applied to review and select antidiabetic medicinal plants used by Aboriginal people in Australia

diabetes-related conditions, such as wounds, ulcers and digestive disorders (Table 1 & 2). Among the 126 species, 29 have been studied for their antidiabetic properties, 26 have been studied both for their antidiabetic and phytochemical properties (Table 1), and 73 species have not been reported for their antidiabetic activities or isolated compounds (Table 2).

Diversity and habit of antidiabetic medicinal plants

The 126 selected medicinal plants (Tables 1, 2) belong to 47 families and 88 genera. Myrtaceae was the dominant family (with 17 species), followed by Fabaceae (14 species), Euphorbiaceae (11 species), and Malvaceae, Proteaceae and Lamiaceae (6 species each) (Fig. 2). With more than 6,000 species, Myrtaceae is found mainly in tropical regions and has been exploited for human use (Hardstaff et al. 2022). Some genera of Myrtaceae that have medicinal purposes are *Eucalyptus*, *Eugenia*, *Melaleuca,* and *Syzygium*. Among the *Syzygium* species, *Syzygium cumini* is known for its antidiabetic properties (Masaenah et al. 2021). This species has thus been studied for its constituents. Other species of the genera *Eucalyptus*, *Eugenia*, and *Melaleuca* have not been reported to have antidiabetic properties.

Shrubs were the most dominant lifeform (54 species), followed by trees (45 species), herbs (18 species), climbers (7 species), epiphytes (2 species), and palm-like plants (1 species) (Fig. 3A). An example of a medicinal shrub is *Melastoma affine* (Melastomataceae), a pioneer shrub species in the rainforests of Australasian rainforests, including those in India, China, Papua New Guinea, Southeast Asia, and Australia (Gross 1993; AVH 2024). An example of a medicinal tree is *Melaleuca leucadendra,* and an example of a medicinal herb is *Cleome viscosa*, whose leaves and young shoots are edible and are used to heal wounds and ulcers (Lassak and McCarthy 2011).

Different parts of the antidiabetic medicinal plants used for treatment

Various parts of plants are indicated as medicinal by the Australian Aboriginal people to treat diabetes-related symptoms, and they are classified into eight categories: 'whole plant,' 'leaf,' 'bark,' 'root,' 'plant exudate,' 'fruit and seed,' 'charcoal and ash,' and 'twig' (Fig. 3B). The 'whole plant' category refers to herbaceous plants where the roots, stems, and leaves are easier to collect than specific parts. The 'leaf' category comprises young leaves, leaf stalks, petioles, and young shoots; the 'bark' category includes outer and inner bark and root bark; the 'root' category includes tap roots, tubers, and bulbs; the 'plant exudate' category includes sap, gum, resin, kinos, and latex; and the 'fruit and seed' category comprises fruits, seeds, kernels, and pods. Leaves were the most commonly used part (38.8%), followed by bark (16.3%), fruit and seeds (11.8%), whole plants (10.7%), plant exudates (10.1%), roots (8.4%), charcoal and ash

Table 1 Australian tropical medicinal plants traditionally used for treating wounds and diabetes-related conditions that are studied for phytochemical composition and/or antidiabetic properties (Cribb and Cribb 1981; Barr et al. 1993; Low 1989, 1990; Clarke 2007; Kyriaziz 1995; Williams 2010; Lassak and McCarthy 2011; Bindon 1996; Maiden 1889; Edgar et al. 1997; Webb 1959; ALA 2024; AVH 2024; APC 2024; WFO 2024; UTP 2024)

Family	Botanical name	Habit	Part(s) used	Conditions or ailments treated	Phytochemical studies/compound isolation	Antidiabetic studies
Acanthaceae	*Avicennia marina* (Forssk.) Vierh.	Tree	Leaves, young shoots, ash, and charcoal of wood	Pain relief, skin lesions and infections, ulcers, sores	Yes	Yes
Apocynaceae	*Cynanchum viminale* subsp. *australe* (R.Br.) Meve & Liede	Shrub	Sap	Bleeding wounds and healing sores	Yes	No
Asteraceae	*Ageratum conyzoides* L.	Herb	Whole plant	Wounds	Yes	Yes
	Pterocaulon serrulatum (Montrouz.) Guillaumin	Herb	Whole plant	Wounds	Yes	No
	Pterocaulon sphacelatum (Labill.) Benth. & Hook.f. ex F.Muell.	Shrub	Leaves	Open wounds, sores, and inflamed eyes	Yes	No
Boraginaceae	*Heliotropium indicum* L.	Herb	Leaves	Skin sores and rheumatism	Yes	Yes
Capparaceae	*Capparis lanceolaris* DC.	Shrub	Bark	Scratches and sores	Yes	No
Cleomaceae	*Cleome viscosa* L.	Herb	Leaves, young shoots (edible)	Counterirritant, wounds, ulcers, and earache	Yes	Yes
Combretaceae	*Terminalia catappa* L.	Tree	Leaves (fruits are edible)	Mouth infections and sore throat	Yes	Yes
Convolvulaceae	*Ipomoea pes-caprae* (L.) R.Br.	Climber	Leaves	Boils, salves, sexually transmitted disease, sores	Yes	No
	Merremia tridentata (L.) Hallier f.	Climber	Whole plant	Sores, skin lesions, wounds	Yes	Yes
Cyperaceae	*Eleocharis dulcis* (Burm.f.) Trin. ex Hensch	Shrub	Whole plant (tubers are edible)	Wounds	Yes	Yes

Table 1 continued

Family	Botanical name	Habit	Part(s) used	Conditions or ailments treated	Phytochemical studies/compound isolation	Antidiabetic studies
Euphorbiaceae Fabaceae	*Acalypha wilkesiana* Müll.Arg.	Shrub	Whole plant	Open sores, sedative	Yes	Yes
	Euphorbia atoto G.Forst.	Shrub	Milky sap	Ulcers	Yes	No
	Euphorbia pilulifera L.	Herb	Leaves. Leaves are also consumed as herbal tea	Pain relief, wounds	Yes	No
	Macaranga tanarius (L.) Müll.Arg.	Shrub	Leaves	Wounds	Yes	Yes
	Acacia auriculiformis A.Cunn. ex Benth.	Tree	Whole plant	Sores, sore eyes, aches, rheumatism, allergy, itching, rashes	Yes	Yes
	Acacia kempeana F.Muell.	Shrub	Leaves	Wounds	No	Yes
	Castanospermum australe A.Cunn. ex Mudie	Tree	Seeds (edible)	Postprandial hyperglycaemia in diabetic patients	Yes	Yes
Flagellariaceae	*Flagellaria indica* L.	Climber	Leaves	Wound healing, sore eyes	No	Yes
Hydrophyllaceae	*Hydrolea zeylanica* (L.) Vahl	Herb	Leaves (young shoots are edible)	Ulcers, wounds	No	Yes
Lamiaceae	*Ajuga australis* R.Br.	Shrub	Leaves	Wounds, ulcers, sores	Yes	No
	Ocimum gratissimum L.	Herb	Whole plant	Hypotension	Yes	Yes
	Ocimum tenuiflorum L.	Shrub	Whole plant	Diarrhoea, dysentery, malaria, skin disease, wounds	Yes	Yes
	Volkameria inermis L.	Shrub	Leaves, bark	Sores, wounds	Yes	Yes
Lauraceae	*Cassytha filiformis* L.	Climber, parasite	Whole plant	Ulcers, inflamed eyes	Yes	Yes
Lecythidaceae	*Planchonia careya* (F.Muell.) R.Knuth	Tree	Bark (fruits are edible)	Wounds, sores	Yes	No
Loganiaceae	*Strychnos lucida* R.Br.	Shrub	Bark, roots, fruits	Skin sores, burns, cuts, wounds	Yes	No

Table 1 continued

Family	Botanical name	Habit	Part(s) used	Conditions or ailments treated	Phytochemical studies/compound isolation	Antidiabetic studies
Malvaceae	*Abutilon indicum* (L.) Sweet	Shrub	Whole plant	Leprosy, ulcers. It also possesses demulcent properties and anti-inflammatory properties	Yes	Yes
	Grewia hirsuta Vahl	Shrub	Roots	Cuts, sores	Yes	Yes
	Hibiscus vitifolius L.	Herb	Roots or tubers	Boils	Yes	Yes
Melastomataceae	*Melastoma affine* D.Don	Shrub	Leaves (fruits are edible)	Diarrhoea, dysentery, burns, ulcers, and wounds	Yes	Yes
Menispermaceae	*Tinospora smilacina* Benth.	Climber	Whole plant	Pain relief, headache, rheumatism, wounds	Yes	No
Moraceae	*Ficus coronata* Spin	Tree	Leaves (syconia are edible)	Wounds	Yes	No
	Ficus racemosa L.	Shrub	Bark, leaves (syconia are a bush food)	Boils	Yes	Yes
Myoporaceae	*Eremophila duttonii* F.Muell.	Shrub	Leaves	Infected cuts, scabies, open sores, ears, inflamed eyes	Yes	No
Myrtaceae	*Eucalyptus camaldulensis* Dehnh.	Tree	Leaves	Wounds and sores	Yes	No
	Eucalyptus microtheca F.Muell.	Tree	Leaves (seeds are edible)	Skin sores	Yes	No
	Melaleuca leucadendra (L.) L.	Tree	Leaves, bark (flowers used for making sweet drinks)	Sedative, respiratory infections, skin diseases	Yes	No
	Syzygium cumini (L.) Skeels	Tree	Leaves (fruits are edible)	Diabetes	Yes	Yes
Orchidaceae	*Cymbidium sp.*	Herb	Leaves	Cuts, sores, and burns	Yes	No
Pandanaceae	*Pandanus tectorius* Parkinson	Tree	Leaves, stems (fruits and kernels are edible)	Cold/flu, hepatitis, dysuria, asthma, boils, cancer, and to alleviate vomiting	Yes	Yes
Phyllanthaceae	*Flueggea virosa* (Roxb.ex Willd.) Royle	Shrub	Whole plant (fruits are edible)	Sores and skin ailments	Yes	No
Poaceae	*Cymbopogon ambiguus* (Hack.) A.Camus	Shrub	Leaves	Wounds and sores	Yes	No
Proteaceae	*Grevillea striata* R.Br.	Shrub	Charcoal of plant, and dried sap from bark	Wounds	Yes	No

Table 1 continued

Family	Botanical name	Habit	Part(s) used	Conditions or ailments treated	Phytochemical studies/compound isolation	Antidiabetic studies
Rhamnaceae	*Ventilago viminalis* Hook.	Climber	Bark, roots	Toothache, rheumatism, swelling, cuts, sores	Yes	No
	Ziziphus oenopolia (L.) Mill.	Shrub	Whole plant	Fresh wounds, ulcers	Yes	Yes
Rubiaceae	*Morinda citrifolia* L.	Tree	Leaves	Wounds, ulcers	Yes	Yes
Sapindaceae	*Dodonaea polyandra* Merr. & L.M.Perry	Tree	Leaves and roots	Pain relief, toothache, cuts, open wounds	Yes	No
	Dodonaea viscosa Jacq.	Shrub	Leaves	Open cuts and wounds	Yes	Yes
Scrophulariaceae	*Eremophila sturtii* R.Br.	Shrub	Leaves	Sores, cuts	Yes	No
Simaroubaceae	*Brucea javanica* (L.) Merr.	Tree	Leaves, roots, and seeds	Dysentery, malaria, pain relief	Yes	Yes
Verbenaceae	*Verbena officinalis* L.	Herb	Whole plant	Wounds	Yes	No

(2.2%), and twigs (1.7%). The ease of collection, availability, and minimisation of plant damage facilitate the frequent use of leaves (Turpin et al. 2022).

Disease categories and methods of treatment preparations

We grouped the diseases or conditions associated with the 126 identified medicinal plants into nine categories (Fig. 4). Among the nine categories, the 'skin sores and infections′ (34%), 'cuts, wounds, and burns′ (32%), and 'boils and ulcers′ (9%) categories were associated with mostly treated diseases. For example, dried and powdered sap collected from damaged areas of *Grevillea striata* bark is sprinkled onto sores, burns, and cuts as a drying agent (Cribb and Cribb 1981). The leaves and twigs of *Acacia translucens* are mashed in water, and the liquid is used to bathe skin sores; a leaf decoction of *Ipomoea pes-caprae* is applied to sores, scabies, bites, and stings (Lassak and McCarthy 2011). 'Toothache and mouthwash′ (3%), 'anti-inflammatory′ (3%), 'rheumatism′ (3%), and 'digestive disorder′ (diarrhoea and vomiting, 2%) were the least commonly treated diseases or conditions. The 'others′ category includes dysentery, malaria, respiratory infection, cold and flu, hepatitis, scabies, sexually transmitted infections (STIs), sedatives, and immune system boosters.

Typically, plant parts were prepared in different forms before application or consumption to treat diseases or conditions. They most commonly prepared decoctions or infusions, chew paste, charcoal, and ash or directly applied fresh materials (Lassak and McCarthy 2011; Williams 2010, 2021; Fern 2014). For example, sap collected from damaged areas of *Grevillea striata* bark is dried and powdered to apply on sores, burns, and cuts as a drying agent (Cribb and Cribb 1981). The leaves, bark, and roots of *Alphitonia excelsa* are mashed or crushed and made into aqueous decoctions or infusions before being applied to wounds or sores (Cribb and Cribb 1981; Lassak and McCarthy 2011). A similar method was applied to the leaves of *Brachychiton diversifolius*, *Pterocaulon sphacelatum*, and *Acacia kempeana* and the bark and roots of *Buchanania arborescens*, *Capparis lanceolaris*, and *Grewia retusifolia* (Lassak and McCarthy 2011; Maiden 1889; Barr et al. 1993). Some plants were prepared by boiling or heating them with seawater or saltwater, such as the inner bark of *Hibiscus tiliaceus* and the whole plant of *Eleocharis dulcis* (Cribb and Cribb 1981; Lassak and McCarthy 2011; Fern 2014).

Table 2 Australian tropical medicinal plants traditionally used for treating wounds and diabetes-related conditions not studied for phytochemical composition and antidiabetic properties (Cribb and Cribb 1981; Barr et al. 1993; Low 1989, 1990; Clarke 2007; Kyriaziz 1995; Williams 2010; Lassak and McCarthy 2011; Bindon 1996; Maiden 1889; Edgar et al. 1997; Webb 1959; ALA 2024; AVH 2024; APC 2024; WFO 2024; UTP 2024)

Family	Botanical name	Habit	Part(s) used	Conditions or ailments treated
Amaryllidaceae	*Crinum arenarium* Herb.	Shrub	Bulbs	Wounds, sores
Anacardiaceae	*Buchanania arborescens* Blume	Tree	Inner bark, sapwood, roots (fruits are edible)	Toothache, mouthwash
	Buchanania obovata Engl.	Tree	Leaves, fruit, bark, sapwood (fruits are edible)	Mouthwash, sore eyes, infected rashes, scabies, skin ulcers
	Semecarpus australiensis Engl.	Tree	Leaves (nuts are edible)	Rheumatism, swellings and redness of skin (allergic reactions)
Apocynaceae	*Alstonia actinophylla* K.Schum.	Tree	Leaves, milky sap	Wounds, sores
	Secamone elliptica R.Br.	Climber	Leaves, stems, milky sap	Wounds
Asteraceae	*Cymbonotus lawsonianus* Gaudich.	Shrub	Leaves	Wounds
Boraginaceae	*Trichodesma zeylanicum* (Burm.f.) R.Br.	Herb or Shrub	Leaves, roots	Wounds, pain relief
Burseraceae	*Canarium muelleri* F.M.Bailey	Tree	Resin	Cuts, sores, chronic ulcers
Combretaceae	*Terminalia hadleyana* W.Fitzg.	Shrub	Leaves (fruits are edible)	Skin sores
	Terminalia muelleri Benth.	Tree	Leaves	Skin sores, scabies
Cupressaceae	*Callitris columellaris* F.Muell.	Tree	Bark, leaves, twigs	Abdominal pain and diarrhoea, sores, cuts
Cycadaceae	*Cycas armstrongii* Miq.	Palm-like	Leaves, stems, seeds	Wounds
Dilleniaceae	*Dillenia alata* (R.Br. ex DC.) Banks ex Martelli	Tree	Leaves	Wounds, sores
Euphorbiaceae	*Croton arnhemicus* Müll.Arg.	Shrub	Inner bark	Headache, infected cuts, skin rashes and sores
	Euphorbia australis Boiss.	Herb	Milky sap	Skin sores
	Euphorbia coghlanii F.M.Bailey	Shrub	Milky sap	Skin sores
	Excoecaria parvifolia Müll.Arg.	Tree	Bark	Sores, cuts
	Homalanthus populifolius Graham	Shrub	Leaves	Wounds and cuts to stop bleeding
	Petalostigma quadriloculare F.Muell.	Shrub	Bark, fruits	Itchy skin, sores, cuts, rabies infection
	Synostemon glaucus F.Muell.	Shrub	Roots	Sores, cuts
Fabaceae	*Acacia ancistrocarpa* Maiden & Blakely	Shrub	Whole plant	Skin sores
	Acacia estrophiolata F.Muell.	Tree	Bark, roots	Sores, boils, scabies, headache, stomach pain, wounds, burns
	Acacia inaequilatera Domin	Shrub	Bark	Skin sores, cuts, rashes. It has an astringent and drying action
	Acacia leptocarpa A.Cunn. ex Benth.	Shrub	Bark, seeds (seeds are edible)	Wounds, sore eyes
	Acacia pellita O.Schwarz	Shrub	Leaves, seeds	Sores
	Acacia translucens A.Cunn. ex Hook.	Shrub	Leaves, twigs	Skin sores, headache
	Bauhinia carronii (F.Muell.) Pedley	Tree	Bark	Sores
	Canavalia rosea (Sw.) DC.	Herb	Root, leaves, and petioles. Seeds and pods are edible	Aches, pains, leprosy, and wounds
	Lysiphyllum cunninghamii (Benth.) de Wit	Shrub	Roots, bark	Wounds, sores
	Sesbania burbidgeae C.L.Gross	Tree	Leaves	Boils
	Sesbania formosa (F.Muell.) N.T.Burb.	Tree	Bark ash (flowers are edible)	Wounds, sores

Table 2 continued

Family	Botanical name	Habit	Part(s) used	Conditions or ailments treated
Goodeniaceae	*Scaevola taccada* (Gaertn.) Roxb.	Shrub	Leaves, bark	Wounds
	Goodenia ovata Sm.	Shrub	Leaves, twigs	Diabetes
Gyrostemonaceae	*Codonocarpus cotinifolius* (Desf.) F.Muell.	Shrub	Leaves, stems	Sores, cuts
Lamiaceae	*Orthosiphon aristatus* (Blume) Miq.	Herb	Whole plant	Diuretic and antihypertensive
	Pityrodia jamesii Specht	Shrub	Leaves	Wounds, sores
Loranthaceae	*Decaisnina brittenii* (Blakely) Barlow	Epiphyte	Whole plant	Wounds, sores
Malvaceae	*Grewia latifolia* F.Muell. ex Benth.	Shrub	Leaves (fruits are edible)	Dysentery, toothache, boils, sores
	Grewia retusifolia Kurz	Shrub	Leaves, roots, bark (fruits are edible)	Wounds, sores, diarrhoea
	Hibiscus tiliaceus L. subsp. *tiliaceus*	Shrub	Inner bark and sapwood	Wounds
Meliaceae	*Owenia vernicosa* F.Muell.	Tree	Bark	Skin sores, open cuts, infected eyes
Moraceae	*Ficus coronulata* Miq.	Tree	Leaves, milky sap of young shoots (bush food)	Sores, cuts
	Ficus opposita Miq.	Shrub	Leaves (bush food)	Bruises, swellings, rheumatism, sores
Myrtaceae	*Calytrix exstipulata* DC.	Shrub	Leaves	Wounds, sores
	Corymbia papuana (F.Muell.) K.D.Hill & L.A.S.Johnson	Tree	Bark, resin	Wounds, sores
	Corymbia ptychocarpa (F.Muell.) K.D.Hill & L.A.S.Johnson	Tree	Leaves	Wounds, sores
	Corymbia terminalis (F.Muell.) K.D.Hill & L.A.S.Johnson	Tree	Leaves, gum from bark and trunk	Wounds, sores
	Eucalyptus crebra F.Muell.	Tree	Bark	Sores
	Eucalyptus dichromophloia (F.Muell.) K.D.Hill & L.A.S.Johnson	Tree	Leaves	Wounds, sores
	Eucalyptus miniata A.Cunn. ex S.Schauer	Tree	Leaves	Skin sores
	Eucalyptus tetrodonta F.Muell.	Tree	Leaves	Sores, cuts
	Eugenia reinwardtiana (Blume) DC.	Tree	Fruits (edible)	Wounds
	Syzygium erythrocalyx (C.T.White) B.Hyland	Tree	Fruits (edible)	Wounds
	Syzygium forte (F.Muell.) B.Hyland	Tree	Bark (fruits are edible)	Sore throat, bronchitis, asthma, thirst, biliousness, dysentery, ulcers
	Syzygium luehmannii (F.Muell.) L.A.S.Johnson	Tree	Fruits (edible)	Sore ears, wounds, skin conditions, immune system booster
	Syzygium suborbiculare (Benth.) T.G.Hartley & L.M.Perry	Shrub	Leaves, fruits (edible)	Chest congestion, cough, wounds, sore ear, toothache
Orchidaceae	*Cymbidium canaliculatum* R.Br.	Herb	Whole plant (fruits and stems are edible)	Wounds
	Dendrobium affine (Decne.) Steud.	Epiphyte	Sticky liquid from pseudobulb	Infected skin lesions, sores
	Dendrobium foelschei F.Muell.	Herb	Sticky liquid from pseudobulb	Infected sores, cuts
Plantaginaceae	*Stemodia viscosa* Roxb.	Herb	Leaves	Wounds
Poaceae	*Cymbopogon procerus* (R.Br.) Domin	Herb	Whole plant	Sores, cuts
Proteaceae	*Grevillea heliosperma* R.Br.	Shrub	Leaves, bark	Sores
	Grevillea pyramidalis A.Cunn. ex R.Br.	Shrub	Bark	Sores
	Hakea arborescens R.Br.	Shrub	Leaves, pods	Scabies, sores
	Hakea macrocarpa A.Cunn. ex R.Br.	Shrub	Charcoal from wood	Open sores, cuts
	Persoonia falcata R.Br.	Shrub	Leaves, bark (fruits are edible)	Diarrhoea, infection and soreness relief, wounds

Table 2 continued

Family	Botanical name	Habit	Part(s) used	Conditions or ailments treated
Rhamnaceae	*Alphitonia excelsa* (Fenzl) Benth.	Tree	Leaves, bark, roots	Sores, rashes, ringworm, headache, toothache
Rubiaceae	*Gardenia pyriformis* A.Cunn. ex Benth.	Shrub	Bark	Aches, sores
Santalaceae	*Exocarpos latifolius* R.Br.	Tree	Leaves	Boils
	Santalum lanceolatum R.Br.	Tree	Leaves, roots (fruits are edible)	Wounds, sores
Sterculiaceae	*Brachychiton diversifolius* (A.Cunn. ex G.Don) F.Muell.	Tree	Leaves, gummy exudate	Wounds, sores, ulcerated skin
	Sterculia quadrifida R.Br.	Tree	Leaves (seeds are edible)	Sore eyes, wounds

The leaves and twigs of *Acacia translucens* are mashed in water, and the liquid is used to bathe skin sores; a leaf decoction of *Ipomoea pes-caprae* is applied to sores, scabies, bites, and stings (Lassak and McCarthy 2011). The fruit of *Grewia retusifolia* is eaten raw to cure diarrhoea and dysentery (Low 1990; UTP 2024). Chewing leaves or drinking an infusion of the mashed roots of *Grewia retusifolia* is also indicated for digestive disorders (Edgar et al. 1997). For example, an infusion of the young leaves of *Flueggea virosa* is drunk for internal pain (Edgar et al. 1997). A decoction from crushed leaves of *Melaleuca leucadendra* is taken orally to ease cough and cold (Low 1990; UTP 2024). Leaves and young shoots of *Avicennia marina* and *Dodonaea polyandra* are chewed and pulped before being applied to wounds. Plant exudates, including resin, oil, latex, and milky sap collected from bark, leaves, or trunks of *Ficus coronulata*, *Euphorbia australis*, and *Corymbia papuana* are directly applied to skin lesion burns, wounds, and cuts (Lassak and McCarthy 2011; Cribb and Cribb 1981; Low 1990). Similarly, charcoal and ash made from the wood of *Grevillea striata* and *Hakea macrocarpa* are also applied to open sores and cuts (Cribb and Cribb 1981; Lassak and McCarthy 2011; Fern 2014). In addition, the seed extracts of *Syzygium cumini* and *Brucea javanica* are considered powerful remedies for treating diabetes (Gajera et al. 2017b, Lassak and McCarthy 2011, Y. Zhan et al. 2020).

Antidiabetic medicinal plants as bush foods

Bush food includes plants, vegetables, fruits, nuts, or berries native to Australia which is used for culinary and medicinal purposes (Mathew 2016, Lawrie 2023). Among the 126 species (Tables 1 & 2), 28 were found to be consumed as bush foods by Australian Aboriginal people. Figure 5 shows the edible plant parts, including fruits (15 species), seeds, pods, and kernels (6 species), flowers, nuts and tubers, leaves and young shoots (2 species each). Only one species was indicated for stems (Fig. 5). Fruits were the most consumed plant part and were typically eaten as raw or roasted form. Examples include the fruits of some *Syzygium* species and others, such as *Grewia retusifolia* and *Persoonia falcata*. The leaves and young shoots (e.g., *Cleome viscosa* and *Hydrolea zeylanica*) were boiled and consumed as vegetables. Young leaves and flowers from *Sesbania formosa* were eaten raw or cooked, while the flowers and leaves of *Melaleuca leucadendra* were taken as herbal tea (Lassak and McCarthy 2011). The pseudobulb (a thickened stem) of *Cymbidium canaliculatum* containing starch is eaten raw or cooked. Another example is *Pandanus tectorius*, whose seeds are consumed raw or cooked, while young flower buds and aerial roots are cooked (Edgar et al. 1997; Kyriaziz 1995; Williams 2010; Fern 2014).

Other commonly consumed parts are the seeds, pods, and kernels. They are either extracted or boiled before consumption. For example, the young pods and seeds of *Canavalia rosea* were boiled or cooked before they are eaten (Fern 2014). Seeds were important source of dietary protein and carbohydrates but can sometimes be harmful if eaten as raw. For example, fresh seeds of *Castanospermum australe*, a native plant of Australia, contain high levels of saponins (Lassak and McCarthy 2011; Fern 2014). To avoid the toxicity of saponins, seeds are finely sliced and soaked in running water for 10 days before roasting and grinding them into a powder (Fern 2014; Maiden 1889). A high content of saponins has cytotoxic activities (Jiang et al. 2018), possesses

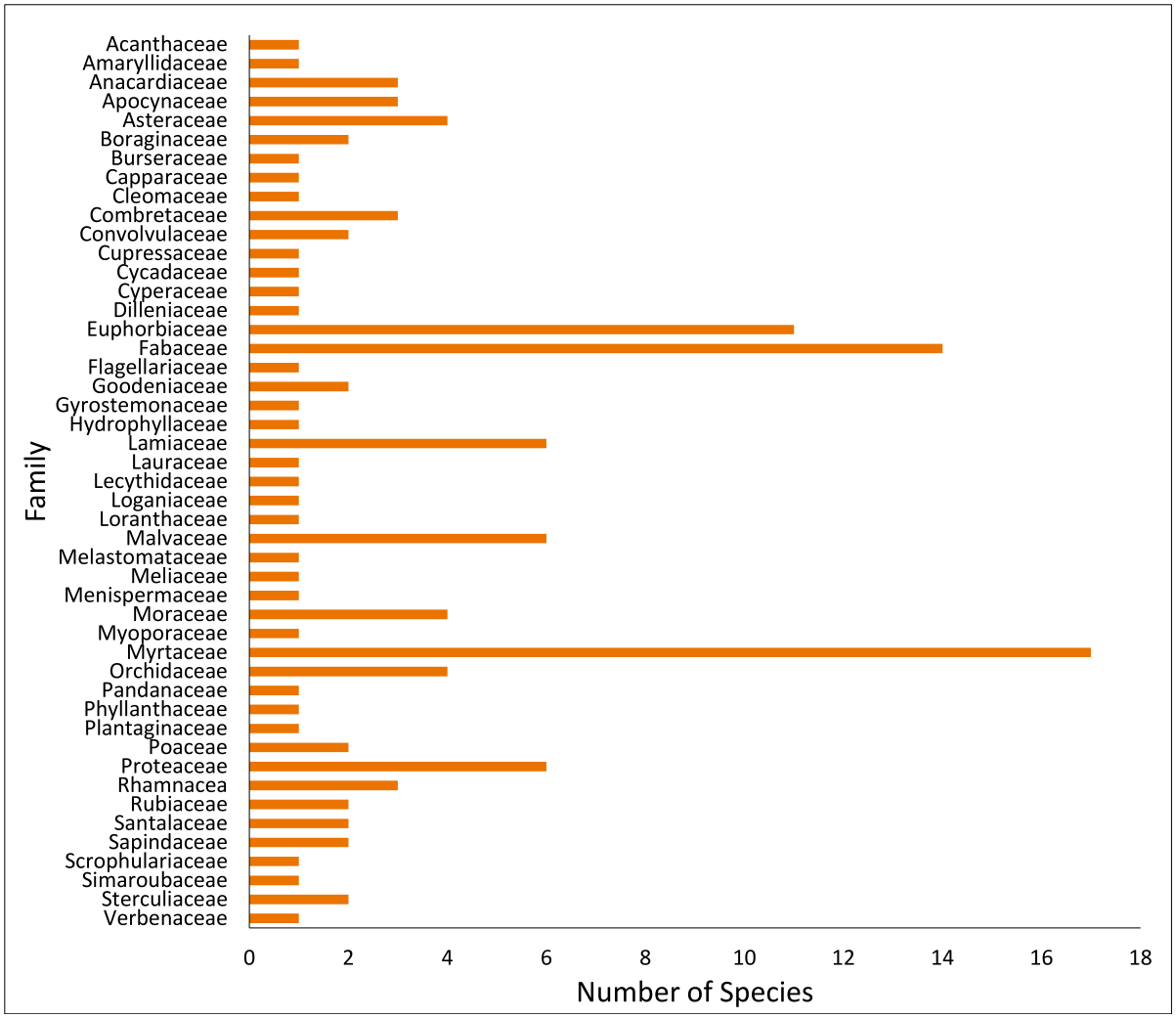

Fig. 2 Diversity of Australian tropical medicinal plants for treating diabetes-related conditions by family

harmful haemolytic toxicity (Zheng et al. 2019), and causes diarrhoea (Lin et al. 2021).

Edible medicinal plants have potential health benefits as nutraceuticals and dietary supplements, particularly for the prevention or treatment of T2D (Xu et al. 2018; Lin et al. 2024). Nutraceuticals are defined as a food or food component that provides medicinal or health benefits, including prevention and treatment of diseases (DeFelice 1995). Due to their established safety profile, nutraceuticals and dietary supplements are associated with low risks of obesity and diabetes (Zhu et al. 2020). Moreover, from a psychological perspective, regular supplementation with consumable plants can improve patient adherence following a T2D diagnosis, as nutraceuticals are generally well received by individuals with chronic conditions (Mahmood et al. 2020; Barry 2018; Piragine et al. 2022). Furthermore, using edible plants rich in active compounds therapeutically could benefit the early stages of T2D. This approach may help slow disease progression, delay the need for synthetic antidiabetic drugs, and reduce the onset of diabetic complications (Piragine et al. 2022). In addition to their potential for lowering glucose levels, antidiabetic medicinal plants possess antioxidant and anti-inflammatory properties that may help prevent

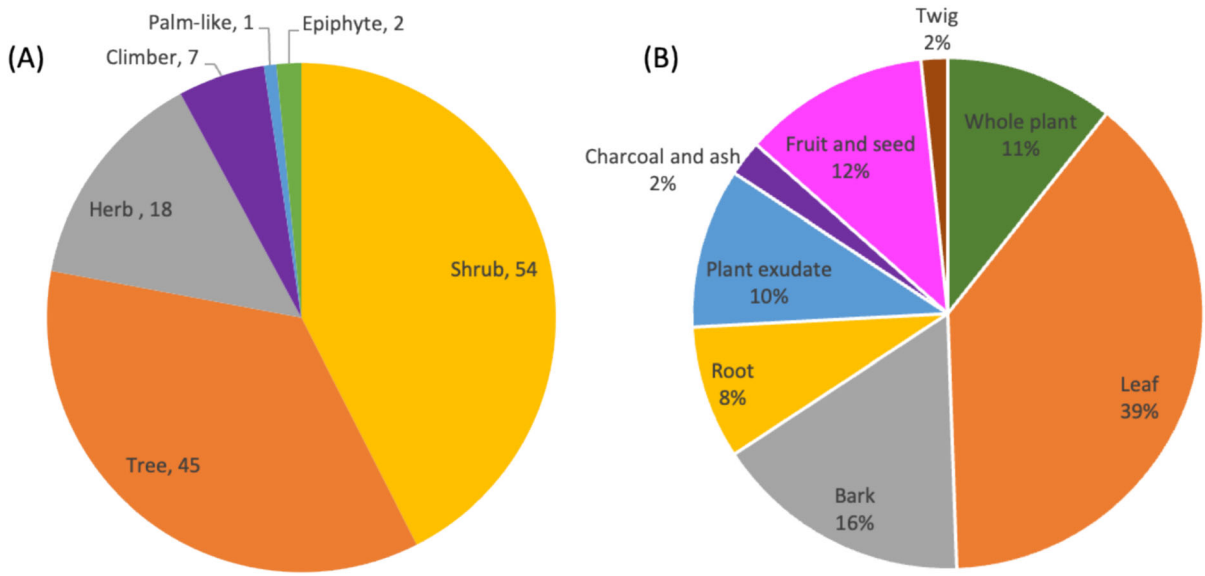

Fig. 3 Habit (A) and plant parts used (B) of Australian antidiabetic tropical medicinal plants

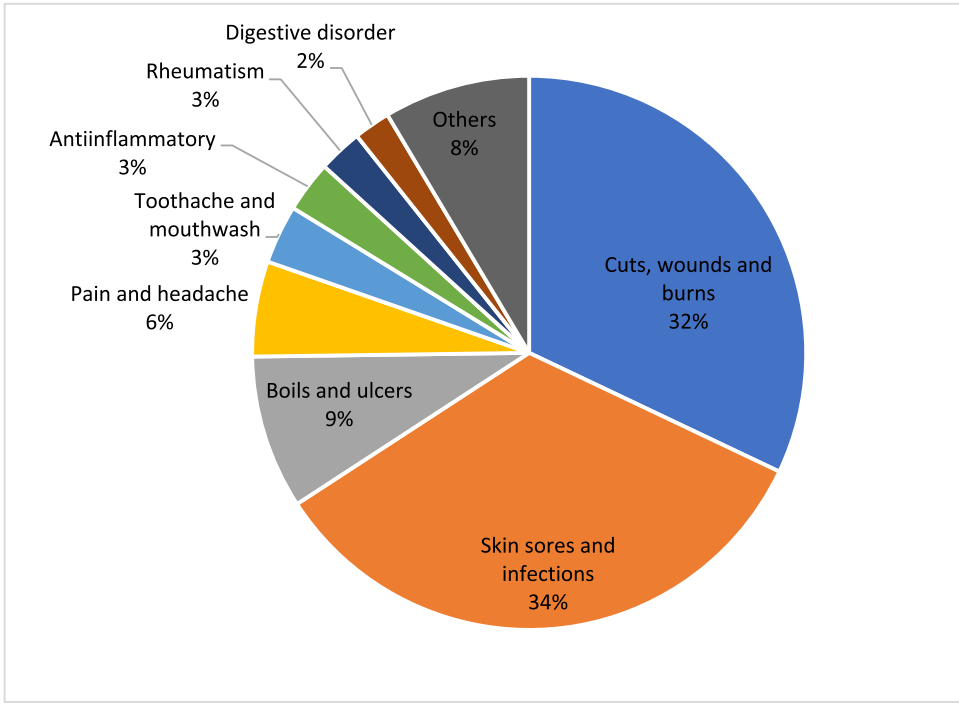

Fig. 4 Categories and percentages of diseases treated by the Australian tropical medicinal plants

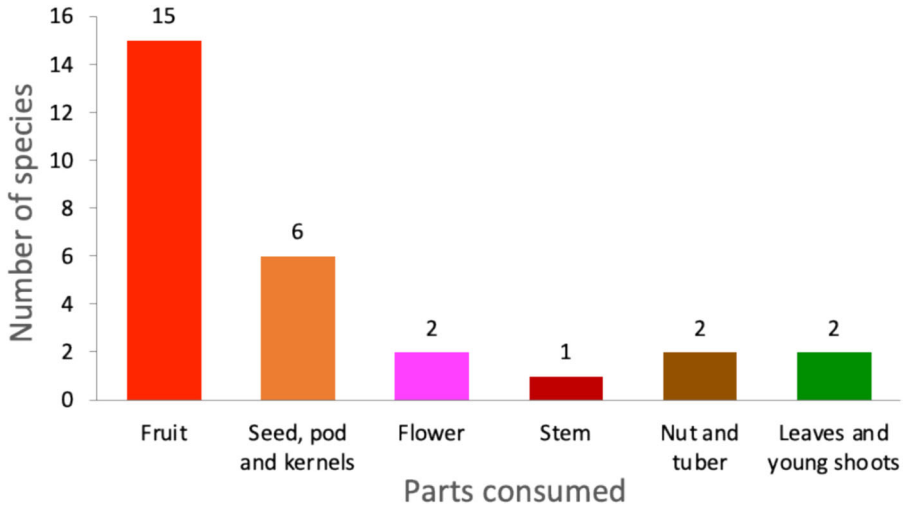

Fig. 5 Different parts of Australian tropical medicinal plants used as bush foods

microvascular and macrovascular complications related to T2D (Piragine et al. 2022; Khan et al. 2013; Subramaniam et al. 2014). Thus, interest in antidiabetic compounds or products derived from medicinal plants is increasing, as they have proven effective in managing diabetes and its complications with minimal side effects (Lin et al. 2024).

Crude extracts and phytochemicals from aboriginal medicinal plants

1. Antidiabetic crude extracts

The in vitro antidiabetic activities of plant crude extracts (Table 3) primarily rely on inhibiting two metabolic enzymes: α-glucosidase and α-amylase. These enzymes are crucial in the pathogenesis of T2D as they play key roles in glucose production and the absorption of carbohydrates during digestion. Therefore, inhibiting these enzymes is a significant strategy in managing blood glucose levels (Oboh et al. 2014; Hamden et al. 2013). Based on half-maximal inhibitory concentration (IC_{50}) values against α-glucosidase and α-amylase enzymes' activities, seed extract of *Syzygium cumini*, fruit extract of *Terminalia catappa*, and root bark extract of *Acalypha wilkesiana* were the three most promising extracts (Fitri Amelia et al. 2024, Laxman Sawant et al. 2015) (Table 3). *Syzygium cumini* seed extract inhibited α-amylase at much lower concentrations than standard acarbose (24.7 µg/mL) (Gajera et al. 2017b). Another enzyme inhibition test focuses on DPP-IV (Dipeptidyl peptidase-IV), which plays a significant role in glucose metabolism. Inhibiting DPP-IV can help normalize blood glucose levels in humans, making it a potential treatment for T2D (Huang et al. 2019; Florentin et al. 2022). For this activity, the seed extract of *C. australe* exhibited higher in vitro inhibitory activity (IC_{50} = 13.96 µg/mL) of DPP-IV compared to the standard Diprotin A (IC_{50} = 1.543 µg/mL).

From the review of crude extracts studies from 29 species (Table 3), crude extracts of *Syzygium cumini*, *Morinda citrifolia*, and *Acalypha wilkesiana* were most widely studied for their in vitro antidiabetic activities. Almost all parts of *Syzygium cumini* have been examined, demonstrating antidiabetic effects, with the leaves and seeds showing superior activities (Mahindrakar and Rathod 2022; Mujawah et al. 2023; Syama et al. 2018; Gajera et al. 2017a, Zheng et al. 2019). The leaves and root bark of *Acalypha wilkesiana* have also been investigated (Oyebode et al. 2018; El-Manawaty and L. Gohar 2018), while the fruits and fermented fruits of *Morinda citrifolia* have been studied for their antidiabetic potential (So-Young Lee et al. 2012; Simamora et al. 2019; Lolok et al. 2023). Traditionally, plant extracts were prepared using water. However, contemporary research on antidiabetic medicinal plants employs various solvents such as methanol, ethanol, water, ethyl acetate, and chloroform. These solvents extract compounds based on their polarity, which affects the bioactivities

Table 3 In vitro activity of Australian tropical antidiabetic medicinal plants

Species	Part studied	Compound/extract/fraction	Dose	In vitro (cell lines/enzyme inhibitions)	Mechanism/activity	References
Abutilon indicum (L.) Sweet	Whole plant	Water extract	100 µg/mL and 500 µg/mL	HCT-116 cells, L6 myocytes	↑ GLUT1 promoter, ↓Insulin resistance via PPARα and PPARγ activation	Krisanapun et al. (2011)
	Leaves	Methanol extract	200–800 µg/mL	3T3L1 cells	↑Glucose uptake/consumption	Lavanya (2022)
		Methanol extract		RIN5F cell lines	↑Insulin release	Lavanya (2022)
Acacia auriculiformis A.Cunn. ex Benth.	Leaves	Methanolic extract	2–20 µg/mL	Enzyme inhibitions	- Inhibited α-glucosidase (94.259%) and α-amylase (95.259%)	Rangra et al. (2021)
	Stem bark	*p*-Propoxybenzoic acid	20 µg/mL	Enzyme inhibitions	- Inhibited α-amylase (IC_{50} = 50 ± 0.45 µg/mL)	Johnson et al. (2022)
	Leaves	α-Spinasterol	5–100 µg/mL	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 8.65 ± 1.71 µg/mL)	Lawal et al. (2020)
Acacia kempeana F.Muell.	Leaves	Ethanolic extract	100 µg/mL	3T3L1 cells	↑Glucose uptake/consumption	Gulati et al. (2015)
Acalypha wilkesiana Müll.Arg.	Leaves	Ethanolic extract	50–250 µg/mL	Enzyme inhibitions	- Inhibited α-glucosidase (EC_{50} = 67.18 ± 7.65 µg/mL) and α-amylase (EC_{50} = 75.35 ± 8.25 µg/mL)	Oyebode et al. (2018)
		Methanolic extract		Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 5.43 ± 0.9 ppm)	May Aly El-Manawaty and Lamiaa Gohar (2018)
	Root bark	Ethanolic extract	50–250 µg/mL	Enzyme inhibitions	- Inhibited α-glucosidase (EC_{50} = 35.75 ± 1.95 µg/mL) & α-amylase (EC_{50} = 6.25 ± 1.05 µg/mL)	Oyebode et al. (2018)
Brucea javanica (L.) Merr.	Seeds	Ethyl acetate fraction	25–500 µg/mL	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 483.93 µg/mL)	Ablat et al. (2017)
		Luteolin	25–500 µg/mL	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 26.41 ± 0.04 µM) and GPα ((IC_{50} = 45.08 ± 0.04 µM)	Abdulwali Ablat et al. (2017)
Castanospermum australe A.Cunn. & C. Fraser	Seeds	70% Ethanolic extract	2.5–80 µg/mL	Enzyme inhibitions	- Inhibited DPP-IV (IC_{50} = 13.96 µg/mL)	Bharti et al. (2012)
		7-Deoxy-6-epi-castanospermine	1 mM	Enzyme inhibitions	- Inhibited yeast α-glucosidase (50%), glucosidase I (35%), intestinal sucrase (30%) and β-galactosidase (20%)	Molyneux et al. (1990a)
		Australine	5.8 µM	Enzyme inhibitions	- Inhibited 50% α-glucosidase and amyloglucosidase	Tropea et al. (1989)

Table 3 continued

Species	Part studied	Compound/extract/fraction	Dose	In vitro (cell lines/enzyme inhibitions)	Mechanism/activity	References
Cleome viscosa L.	Whole plant	FD fraction	20–100 µg/mL	Enzyme inhibitions	- Inhibited α-amylase (IC_{50} = 25.93 ± 0.83 µg/mL) and α-glucosidase (IC_{50} = 48.76 ± 0.96 µg/mL)	Suresh et al. (2020)
Dodonaea viscosa Jacq.	Aerial part, leaves, stem, root	Crude extracts from 14 different solvents	4 mg/10 µL DMSO	Enzyme inhibition	- Moderately inhibited α-amylase	Malik et al. (2022)
Eleocharis dulcis (Burm.f.) Trin. ex Hensch.	Chestnuts	Ethanolic extract	2000 ppm	Enzyme inhibition	- Inhibited α-glucosidase (65.74%)	Baehaki et al. (2021)
Ficus racemosa L.	Stem bark	Aqueous extract	1–5 mg/mL	Yeast cells	↑Glucose uptake/consumption	Ahmed and Urooj (2010)
Grewia hirsuta Vahl	Leaves	Chloroform/methanol fraction	100 µg/mL	Enzyme inhibition	- Inhibited α-amylase (52.73%)	Abirami and Natarajan (2014)
	Leaves	(4*Z*, 12*Z*)-cyclopentadeca-4, 12-dienone	NA	3T3-L6 cells	- Inhibited α-amylase and α-glucosidase	Natarajan et al. (2015)
Macaranga tanarius Müll.Arg.	Leaves	Macatannin A	NA	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 0.80 mM)	Gunawan-Puteri and Kawabata (2010)
		Macatannin B	NA	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 0.55 mM)	Gunawan-Puteri and Kawabata (2010)
		Chebulagic acid	NA	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 1.0 mM)	Gunawan-Puteri and Kawabata (2010)
		Corilagin	NA	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 2.63 mM)	Gunawan-Puteri and Kawabata (2010)
		Mallotinic acid	NA	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} > 5.0 mM)	Gunawan-Puteri and Kawabata (2010)
	Fruits	Isonymphaeol B & 3′-geranyl naringenin	30 µM	L6 rat myoblasts	↑Glucose uptake, ↑AMPK phosphorylation, ↑Glut1 mRNA expression, ↑Plasma membrane GLUT1 protein level	Natsume et al. (2021)
Merremia tridentata (L.) Hallier f.	Stem	50% Ethanol extract	1 mg/mL	Enzyme inhibitions	- Inhibited α-amylase (IC_{50} = 1.61–1.72 mg/mL) and α-glucosidase (IC_{50} = 0.24–0.44 mg/mL)	Vo Van et al. (2022)
		Flavonoid-rich fraction	0.1 mg/mL	Enzyme inhibitions		

Table 3 continued

Species	Part studied	Compound/extract/fraction	Dose	In vitro (cell lines/enzyme inhibitions)	Mechanism/activity	References
Morinda citrifolia L.	Fruits	Fermented fruit juice	23.86 µg GAE/mL	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 28.99 ± 4.31 µg/mL)	Simamora et al. (2019)
		Ethanolic extract	150, 75, 37.5, 18.75, and 9.375 ppm	Enzyme inhibitions	- Inhibited α-amylase (IC_{50} = 14.16 ± 5.72 ppm)	Lolok et al. (2023)
		Stigmasterol	150, 75, 37.5, 18.75, and 9.375 ppm	Enzyme inhibitions	- Inhibited α-amylase (IC_{50} = 10.29 ± 0.76 ppm)	Lolok et al. (2023)
	Whole plant	Lirioresinol B, episesamin 2,6-dicatechol	20 µM	3T3-L1 adipocyte cells	↑2-NBDG uptake	Nguyen et al. (2013)
		Lirioresinol B dimethyl ether, Ursolic acid	40 µM			
	Fruits	Fermented *M. citrifolia* 70% ethanolic extract (FMCE)	50–400 µg/mL	C2C12 cells	↑Glucose uptake via activated-AMPK & PPAR-γ	So-Young Lee et al. (2012)
Ocimum gratissimum L.	Leaves	Pap water extract	0.1–2.5 mg/mL	Enzyme inhibitions	- Inhibition of α-amylase (IC_{50} = 0.47 mg/mL) and α-glucosidase (IC_{50} = 9.09 µg/mL)	Agunbiade et al. (2024)
Pandanus tectorius Parkinson	Fruits	(*Z*)-4H-hydroxy-3-(4-hydroxy-3-methylbut-2-en-1-yl) benzaldehyde	NA	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 192.4 ± 0.2 µM)	Mai et al. (2015)
		p-Hydroxybenzaldehyde	NA	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 133.1 ± 0.1 µM)	
		Syringaldehyde	NA	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 125.3 ± 0.3 µM)	
		(*E*)-Ferulaldehyde	NA	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 36.5 ± 0.1 µM)	
		(*E*)-Sinapinaldehyde	NA	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 69.5 ± 0.4 µM)	
		Vanillin	NA	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 81.5 ± 0.2 µM)	

Table 3 continued

Species	Part studied	Compound/extract/fraction	Dose	In vitro (cell lines/enzyme inhibitions)	Mechanism/activity	References
Syzygium cumini (L.) Skeels	Leaves	Aqueous extract	10–100 µg/mL	Enzyme inhibitions	- Inhibited α-amylase (IC_{50} = 8.3 µg/mL) and α-glucosidase (IC_{50} = 6.64 µg/mL)	Mahindrakar and Rathod (2022)
	Bark	Chloroform fraction	0.2 µg/mL	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 77.09 ± 1.98 µM)	Mujawah et al. (2023)
		Friedelin	0.2 µg/mL	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 17.54 ± 1.54 µM)	
	Fruits	Methanol extracts of kernel, seeds, seed coat, & pulp	0.1–300 µg/mL	Enzyme inhibitions	- Inhibited α-amylase (IC_{50} = 8.3, 12.9, 50.8, 270 µg/mL, respectively)	Gajera et al. (2017b)
	Seeds	Ethyl acetate fraction	Up to 100 µg/mL	Enzyme inhibitions	- Inhibited PTP1B (IC_{50} = 26.36 µg/mL) and AR (IC_{50} = 2.50 µg/mL)	Sawant et al. (2015)
		Gallic acid		Enzyme inhibitions	- Inhibited AR (IC_{50} = 0.77 µg/mL)	
		Valoneic acid dilactone			- Inhibited AR (IC_{50} = 0.075 µg/mL)	
		Rubuphenol			- Inhibited AR (IC_{50} = 0.165 µg/mL)	
		Ellagic acid			- Inhibited AR (IC_{50} = 0.12 µg/mL)	
		70% Methanol fraction	0–60 µg/mL	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 1.7 mg/mL) and α-amylase (IC_{50} = 7.62 mg/mL)	Syama et al. (2018)
		Methanol fraction	10 µg/mL		- Inhibited DPP-IV (88.1%)	
		70% Methanol fraction	10 µg/mL	L6 myocytes	↑2-NBDG uptake (26.9%)	
Terminalia catappa L.	Fruits	Methanol extract	31.25, 62.5, 125, 250, 500, 1000 µg/mL	Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 1.04 ± 0.02 mg/mL) and α-amylase (IC_{50} = 0.19 ± 0.06 mg/mL)	Amelia et al. (2024)
		Ethyl acetate extract		Enzyme inhibitions	- Inhibited α-glucosidase (IC_{50} = 3.20 ± 1.72 mg/mL) and α-amylase (IC_{50} = 0.20 ± 0.03 mg/mL)	

AMPK 5′ AMP-activated protein kinase, *AR* aldose reductase, *DPP-IV* dipeptidyl peptidase-IV, EC_{50} half-maximal effective concentration, IC_{50} half-maximal inhibitory concentration, *GLUT1* glucose transporter 1, *GPα* the P4 specific replication protein, *PPARα* peroxisome proliferator-activated receptor-alpha, *PPARγ* peroxisome proliferator-activated receptor-gamma, *PTP1B* protein tyrosine phosphatase 1B, *2-NBDG* 2-[N-(7-nitrobenz-2-oxa-1,3-diazol-4-yl) amino]-2-deoxy-D-glucose

of the extracts. For instance, *Terminalia catappa* fruit extracted using methanol and ethyl acetate exhibited different antidiabetic activities in vitro, with the methanol extract showing higher activity (Fitri Amelia et al. 2024). Similar results were observed with *Acalypha wilkesiana* leaves extracted using methanol and ethanol, where the methanol extract demonstrated better activities (Oyebode et al. 2018; El-Manawaty and L. Gohar 2018).

The mechanism of action of plant crude extracts was also studied by using various cell lines (Table 3, Fig. 6). These assays target receptors involved in insulin signalling pathways. For example, the aqueous extract of *Abutilon indicum* increased glucose utilisation via glucose transporter-1 (GLUT1) (Chutwadee Krisanapun et al. 2011). Fermented fruit extract of *Morinda citrifolia* enhanced glucose uptake by activating adenosine 5′-monophosphate-activated protein kinase (AMPK) (So-Young Lee et al. 2012). Methanol and water extracts of *Orthosiphon aristatus* aerial parts scavenged the oxidants and boosted the translocation of glucose transporter-4 (GLUT4) to the plasma membrane in skeletal muscles (Bassalat et al. 2023), while fruit extract from *Pandanus tectorius* reduced insulin resistance by activating the AMPK–AS160–GLUT4 pathway in skeletal muscles and suppressing gluconeogenesis and lipogenesis in the liver (Fig. 6) (Wu et al. 2014).

Most in vivo antidiabetic studies of plant crude extracts were conducted in T2D rodent models. Chemically-induced diabetic rodent models using streptozotocin (STZ) or alloxan chemicals with glibenclamide or metformin as standard drugs were the most common in in vivo studies (Table 4). From in vivo studies, crude extracts lowered blood-glucose levels, reduced hemoglobin A1c (HbA1c) levels, and improved insulin sensitivity. For example, *C. australe* seed extract (100 and 150 mg/kg bw) significantly reduced the elevated blood glucose levels and improved Haemoglobin A1c (HbA1c) and insulin levels in T2D rats ($p \leq 0.001$) (Sudhanshu Kumar Bharti et al. 2012). Similarly, ethanol extract from leaves and flowers of *Melastoma affine* (150 and 300 mg/kg bw) lowered blood glucose levels and

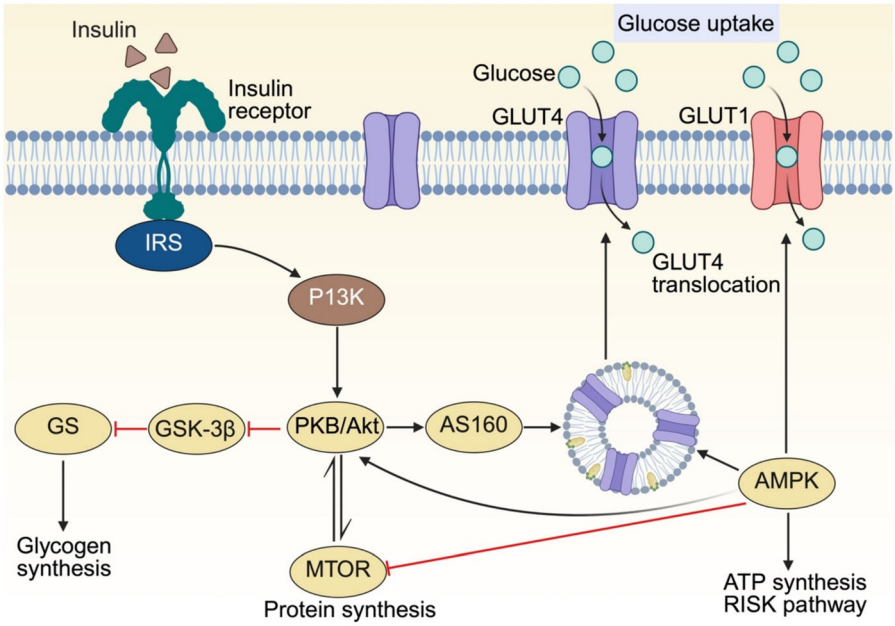

Fig. 6 Targeted molecular modes of crude extracts and isolated compounds in the insulin signalling pathway (Litwiniuk et al. 2021; Izundegui and Nayor 2022). Insulin works by interacting with specific receptors on target cells, known as insulin receptors (IRs), which include insulin receptor substrate (IRS). When insulin binds to these receptors, it activates an enzyme called phosphatidylinositol 3-kinase (PI3K), which triggers a series of reactions leading to the activation of another enzyme, protein kinase B (PKB or AKT). AKT then modifies a protein called glycogen synthase kinase-3 beta (GSK-3β) by adding a phosphate group at the Ser9 site, which reduces its activity. This PI3K/AKT/GSK-3β signalling pathway plays a critical role in insulin signalling and is crucial for regulating glycogen synthesis (Litwiniuk et al. 2021; Izundegui and Nayor 2022)

Table 4 In vivo activity of Australian Tropical antidiabetic medicinal plants

Species	Part studied	Compound/ extract/fraction	Dose	In vivo model	Activity/mechanism of action	References
Abutilon indicum (L.) Sweet	Leaves	Methanol extract	500 mg/kg bw	Wistar rats (STZ-induced)	↓Plasma glucose level, ↓ ∝ -glucosidase	Adisakwattana et al. (2009)
		Ethanol extract	400 mg/kg bw	Wistar rats (normal)	↓Blood glucose level, ↑GLUT1 activity, ↑PPARγ activation	Seetharam et al. (2002)
	Whole plant	Aqueous extract	0.25 & 0.5 g/kg bw	Wistar rats (STZ-induced)	↓Postprandial plasma glucose level	Krisanapun et al. (2011)
		Aqueous extract	0.5 & 1 g/kg bw	Wistar rats, Swiss Albino mice (STZ-induced)	↓Plasma glucose level	Krisanapun et al. (2009)
Acacia auriculiformis A.Cunn. ex Benth.	Bark	70% Acetone extract	200 & 400 mg/kg bw	Sprague-Dawley (SD) albino rats (alloxan monohydrate-induced)	↓Blood glucose level	Sathya and Siddhuraju (2013)
	Empty pod		100 & 200 mg/kg bw			
Acalypha wilkesiana Müll.Arg.	Roots	Methanol extract	200 & 400 mg/kg bw	Wistar rats (alloxan monohydrate-induced)	↓FBG level, ↓Serum TC, ↓Serum TG, ↓SGOT, ↓SGPT	Odoh et al. (2014)
Ageratum conyzoides L.	Leaves	Aqueous extract	500 mg/kg bw	Rats (alloxan-induced)	↓FBG level	Agunbiade et al. (2012)
	Leaves, stems, and roots	Methanol extract	100 mg/kg bw	Wistar rats (STZ-inducd)	↓FBG level, ↓TC, ↓LDL	Atawodi et al. (2017)
Avicennia marina (Forssk.) Vierh.	Leaves and fruits	Aqueous extract	30 mg/kg bw	Rats (STZ-induced)	↑Serum insulin, ↓Serum glucose level	Kamaei and Moghadamnia (2021)
	Leaves	80% Ethanol extract	100 mg/kg bw, 200 mg/kg bw	Wistar rats (alloxan monohydrate-induced)	↓Bax, ↓Bcl-2, ↓Caspase-9, ↓MDA, ↓HOdG-8, ↓Serum TNF, IL-1β, & IL-6	Sadoughi and Hosseini (2020)
Brucea javanica (L.) Merr.	Seeds	Ethyl acetate fraction	25 & 50 mg/kg bw	SD rats (STZ-induced)	↓Blood glucose level, ↑Insulin, ↑Glycogen, ↓Oxidative stress & inflammation, ↓Lipids level	Abdulwali Ablat et al. (2017)
		96% Ethanol extract	30 mg/kg bw	Wistar rats (Alloxan-induced)	↓FBG level, ↑Insulin secretion, ↑Body weight, β-cells in Islets of Langerhans	Muliasari et al. (2019)

Table 4 continued

Species	Part studied	Compound/ extract/fraction	Dose	In vivo model	Activity/mechanism of action	References
Cassytha filiformis L.	Whole plant	Water, ethyl acetate (EtOAc) and butanol (BuOH) fractions	10 mg/kg bw	Mice (Alloxan-induced)	↓Blood glucose level	Armenia et al. (2016)
	Aerial parts	80% Methanol extract fractions	600 mg/kg bw	Albion mice (Alloxan monohydrate-induced)	↓FBG level, ↓Serum MDA, ↓TC	Nwaehujor et al. (2021)
Castanospermum australe A.Cunn. & C.Fraser	Seeds	70% Ethanol extract	100 & 150 mg/kg bw	Wistar rats (Poloxamer-407-induced)	↓Blood glucose level, ↓HbA1c, ↓Insulin, ↓HOMA-R	Sudhanshu Kumar Bharti et al. (2012)
Cleome viscosa L.	Whole plant	Ethanol extract	100, 200, & 400 mg/kg bw	Wistar rats (STZ-induced)	↓LPO, ↓Lipids, ↓Oxidative stress	Rao et al. (2014)
Clerodendrum inerme Gaertn.	Leaves	45% Ethanol extract	343 & 686 mg/kg bw	Swiss Albino mice	↓Plasma glucose level, ↓MDA in liver & kidney, ↓Oxidation stress, ↑Pancreatic β-cells	Ly et al. (2019)
		Ethanolic extract	400 mg/kg bw	Wistar rats (STZ-induced)	↓Blood glucose level	Bharat Bhushan et al. (2015)
Dodonaea viscosa Jacq.	Leaves	Hydromethanolic extract	500 mg/kg bw	Rabbits (Alloxan monohydrate-induced)	↓Body weight, ↓Blood glucose level	Akhtar et al. (2011)
		Methanol extract	150 & 300 mg/kg bw	Albino Wistar rats (STZ-induced)	↓Blood glucose level, ↓Proinflammatory cytokines, ↑Insulin level	Jangra et al. (2011)
	Aerial parts	Aqueous extract	400 mg/kg bw	Wistar rats	↓Blood glucose level	Veerapur et al. (2010)
		Polar fraction of ethanol extract	200 mg/kg bw		↓Blood glucose level	
		Viscosol	33 mg/kg bw	C57BL/6 mice (HFD, STZ-induced0	↓FBG level, ↑Body weight, ↑Liver profile, ↓Oxidative stress, ↓PTP1B expression	Sohail et al. (2022)

Table 4 continued

Species	Part studied	Compound/ extract/fraction	Dose	In vivo model	Activity/mechanism of action	References
Ficus racemosa L.	Stem bark	Methanol extract	200 and 400 mg/ kg bw	Wistar Albino rats (alloxan-induced)	↓Blood glucose level	Bhaskara Rao et al. (2002)
		Ethanol extract	200 and 400 mg/ kg bw	Wistar Albino rats (STZ-induced)	↓Blood glucose level, ↓Lipid level, ↓Creatine kinase, ↓LDH, ↓CRP, ↓Creatinine, ↓Blood urea nitrogen, ↓MDA, ↓Collagen, ↓Albumin	Joshi et al. (2016)
		95% Ethanol extract	300 mg/kg bw	Wistar Albino rats (alloxan monohydrate-induced)	↓Blood glucose level, ↓Lipids, ↓Lipoproteins	Sophia and Manoharan (2007)
	Fruits	α-Amyrin acetate	100 mg/kg bw	Albino rats (STZ-induced)	↓Blood glucose level	Narender et al. (2009)
	Leaves	β-Sitosterol, lanosterol	100 mg/kg bw	Wistar Albino rats (STZ-induced)	↓Blood glucose level, ↓Serum lipids, ↓HDL, ↓Oxidative stress	Kushwaha et al. (2015)
Flagellaria indica L.	Aerial part	Ethanol extract	250 & 500 mg/ kg bw	Swiss Albino mice	↓Blood glucose level	Karmakar et al. (2021)
Heliotropium indicum L.	Whole plant	Methanol fraction	750 mg/kg bw	Wistar Albino rats (STZ-induced)	↓Blood glucose level	Mohammad et al. (2014)
Hibiscus vitifolius L.	Flowers	Gossypin	20 mg/kg bw	Wistar Albino rats (STZ-induced)	↓Blood glucose level, ↑Plasma insulin, ↓HbA1c, ↑Glycogen content, ↓Plasma proteins, ↓Blood urea	Venkatesan and Sorimuthu Pillai (2012)
Hydrolea zeylanica (L.) Vahl.	Leaves	Hydroalcoholic extract fraction	400 mg/kg bw	Wistar Albino rats (STZ-induced)	↑Glucose homeostasis, ↓Insulin resistance, ↓Inflammatory markers, ↑GLUT2 & GLUT4 expression	Swain et al. (2024)
Macaranga tanarius Müll.Arg	Leaves	Hydromethanolic fraction	50 & 100 mg/ kg bw	db/db mice (C57BLKS/J Iar- + Leprdb/ + Leprdb)	↓Nephropathy, ↓Fibronectin & collagen IV expression	Hsu et al. (2023)
Melastoma affine D.Don	Leaves, flower	Ethanol extract	150 & 300 mg/ kg bw	Wistar Albino rats (alloxan monohydrate-induced)	↑Body weight, ↓Blood glucose level, ↓HbA1c	Balamurugan et al. (2014)

Table 4 continued

Species	Part studied	Compound/ extract/fraction	Dose	In vivo model	Activity/mechanism of action	References
Merremia tridentata (L.) Hallier f.	Roots	Aqueous extract	50 mg/kg bw	Wistar Albino rats (STZ-induced)	↓Blood glucose level, ↑Body weight, ↑Serum insulin, ↓TC, ↓Glycogen content, ↓Serum TG, ↓LPO	Arunachalam and Parimelazhagan (2012)
	Stem	Ethanol extract	100 mg/kg bw	Swiss Albino mice (alloxan-induced)	↓Blood glucose level, ↑Body weight	Vo Van et al. (2022)
Morinda citrifolia L.	Fruits	Ethanol extract	300 mg/kg bw	Wistar Albino rats (STZ-induced)	↓Blood glucose level, ↓HbA1c, ↓Blood urea, ↓Serum creatinine, ↓Plasma insulin, ↓Plasma hemoglobin	Mahadeva Rao and Subramanian (2009)
	M. citrifolia fermented by Cheonggukjang (FMC)	70% Ethanol extract	Fed AIN-93G with 0.4% FMC	KK-Ay/TaJcl mice (banaba-fed)	↓HbA1c level, ↑Insulin sensitivity, ↓LDL-c, ↓Serum TG	Lee et al. (2012)
	Leaves	Aqueous extract	400 mg/kg bw	Wistar rats (Dexamethasone-induced)	↓Body weight, ↓FBG level, ↓Insulin, ↓HOMA-IR	Shittu et al. (2021)
Ocimum gratissimum L.	Leaves	Chicoric acid	3 mg/kg bw	Swiss mice (STZ-induced)	↓Blood glucose level	Casanova et al. (2014)
		Leaf decoction	10% p/v	Swiss mice (STZ-induced)	↓Blood glucose level	Casanova et al. (2014)
		Aqueous extract	500 mg/kg bw	Wistar rats (STZ-induced)	↓Blood glucose level	A et al. (2007)
Ocimum tenuiflorum L.	Leaves	Methanol extract	1 g/kg bw	SD rats (STZ-induced)	↓FBG level	Mousavi et al. (2016)
		60% Ethanol extract	250 & 500 mg/kg bw	Wistar Albino rats (STZ-induced)	↓Body weight, ↓Blood glucose level, ↓Serum TC, ↓TG, ↓LDL-c, ↓VLDL-c	Parasuraman et al. (2015)
Pandanus tectorius Parkinson	Fruit	70% Ethanol fraction	50–200 mg/kg bw	C57BL/6 (HFD)	↓Body weight, ↓FBG level, ↓Insulin, ↑GLUT4 expression & translocation, ↓Glucose & gluconeogenic precursors, ↓Gluconeogenic enzyme G6Pase & PEPCK expressions	Wu et al. (2014)

Table 4 continued

Species	Part studied	Compound/ extract/fraction	Dose	In vivo model	Activity/mechanism of action	References
Syzygium cumini (L.) Skeels	Fruits	Methanol extract	200 mg/kg bw	C57BL/6 (HFD)	↓Blood glucose level, ↑Insulin sensitivity, ↑Glucose tolerance, ↓Hepatic injury, ↓Nephrotoxicity, ↓Lipid markers (TC, TG, LDL-c, VLDL-c levels), ↓Body weight, ↓Adiposity	Thiyagarajan et al. (2024)
	Seeds	Hydroethanolic extract	75 mg/kg bw	Wistar Albino rats (alloxan monohydrate-induced)	↓Blood glucose level, ↑Body weight	Gopal Thiyagarajan et al. (2024)
		96% Ethanol extract	10% in a 1% CMC-Na suspension	Wistar rats (alloxan-induced)	↓Blood glucose level	Dira (2022)
		Cuminoside	50 mg/kg bw	Wistar Albino rats (Tween 80-induced)	↓FBG level, ↓LDL, TC, TG, ↑Hepatic enzymes (AST, ALT, LDH) levels	Farswana et al. (2009)
		Mycaminose	50 mg/kg bw	Wistar rats (STZ-induced)	↓Blood glucose level	Kumar et al. (2008)
Terminalia catappa L.	Fruits	Aqueous extract	42 mg/kg bw	Wistar Albino rats (alloxan-induced)	↓Blood glucose level, ↓Body weight, ↓Serum cholesterol, TG, LDL-c, HDL-c	Nagappa et al. (2003)
		Petroleum ether extract	68 mg/kg bw			
		Methanol extract	40 mg/kg bw			
	Leaves	Ethanol extract	50 mg/kg bw	BALB/c mice (STZ-induced)	↑Body weight, ↑Tissue glucose tolerance, ↑Langerhans islet diameter, ↓FBG level	Hayaza et al. (2019)
		Aqueous extract	400 & 800 mg/kg bw	Wistar rats (HFD)	↑Insulin resistance, ↑Glucose transport, ↑PI3K/AKT signalling	Iheagwam et al. (2022)
Ziziphus oenoplia (L.) Mill.	Fruits	Ethanol extract	100, 200, & 400 mg/kg bw	Rats (STZ-induced)	↓Blood glucose level, ↓TC, ↓TG, ↓LDL	Goyal and Jeyabalan (2021)

Table 5 Clinical studies of Australian tropical antidiabetic medicinal plants

Species	Part studied	Extract/fraction	Dose	Treatment frequency	In vivo model	Activity/ mechanism of action	References
Eleocharis dulcis (Burm.f.) Trin. ex Hensch.	Fruits	Fruits powder mixed with *Brassica rapa* roots powder	500 g with salad (orally)	Once per day for 3 weeks	T2D patients	↓Blood glucose level	Arif et al. (2022)
Morinda citrifolia L.	Fruits	Juice	2 ml/kg bw	Once per day for 8 weeks	T2D patients	↓FBG level, ↓HbA1c level, ↓hs-CRP	Algenstaedt et al. (2018)

hs-CRP high sensitivity C-reactive protein, *HbA1c* Hemoglobin A1c, *T2D* type 2 diabetes

HbA1c in alloxan-induced diabetic rats (Balamurugan et al. 2014). *Syzygium cumini* seed extract demonstrated significant antidiabetic effects by reducing blood glucose levels in both chemically-induced and high-fat diet (HFD)-induced rodent models of experimental T2D at various dosages of body weight (bw) (Gopal Thiyagarajan et al. 2024). Moreover, some crude extracts from medicinal plants were further clinically tested in diabetic patients (Table 5). For example, fruit extract of *Eleocharis dulcis* (mixed with *Brassica rapa* root) and *Morinda citrifolia*, has been tested in T2D patients and showed blood glucose levels reduction (Arif et al. 2022; Algenstaedt et al. 2018) (Table 5).

In vivo testing in diabetic animal models have also evaluated the effectiveness of crude extracts in mitigating T2D-related complications, including cardiovascular diseases, diabetic retinopathy, and liver and kidney injuries (Table 4). Studies have shown that ethanol extract of *Ocimum tenuiflorum* leaves (250 and 500 mg/kg bw) and *Ziziphus oenoplia* fruits (100, 200, and 400 mg/kg bw) reduced lipid profile parameters, such as total triglycerides, total cholesterol, low-density lipid cholesterol (LDL-c) and high-density lipid cholesterol (HDL-c) (Parasuraman et al. 2015; Goyal and Jeyabalan 2021). These parameters are crucial for assessing hypercholesterolemia, a condition linked to increased cardiovascular disease risk in T2D patients (Khil et al. 2023). Additionally, a study observed cardiovascular risk reduction in diabetic rats treated with *Ficus racemosa* stem bark ethanol extract (200 and 400 mg/kg bw), which decreased the expression of marker proteins creatine kinase and creatinine (Joshi et al. 2016). For diabetic retinopathy, the expression of apoptotic factors Bax and Bcl-2, a marker of the condition (Khalfaoui et al. 2010), was reduced by *Avicennia marina* ethanol leaves extract (100 and 200 mg/kg bw) (Sadoughi and Hosseini 2020). Some plant crude extracts also reduced the risk of liver and kidney injuries. For instance, methanol extract of *Acalypha wilkiseana* root decreased levels of serum glutamate pyruvate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT), key enzymes linked to liver health (Odoh et al. 2014), and *Sysygium cumini* fruit extract lowered nephrotoxicity (hepatic injury) (G. Thiyagarajan et al. 2024). *Macaranga tanarius* leaves extract, and *Morinda citrifolia* fruit extract reduced the risk of kidney injury (nephropathy) by lowering some markers, including fibronectin and collagen IV expressions and serum creatine levels (Hsu et al. 2023; Mahadeva Rao and Subramanian 2009). Furthermore, the extract of *S. cumini* and *Avicennia marina* showed recovery from histological hepatic and kidney injury (Sadoughi and Hosseini 2020, G. Thiyagarajan et al. 2024).

2. Antidiabetic phytochemicals

A total of 374 compounds from 26 Australian tropical medicinal plant species have been isolated and characterised thus far (Table 6). Of the total 374 compounds, 51 compounds from 17 medicinal plant species have undergone in vitro and/or in vivo testing to confirm their antidiabetic properties and ethnopharmacological applications (Tables 3 & 4). A total of 16 compounds were identified as promising antidiabetic drug leads (Fig. 7). The most tested compounds were isolated from *Brucea javanica*, *Syzigium cumini*, *Macaranga tanarius,* and *Pandanus tectorus.* Luteolin (**1**) (isolated from *Brucea javanica*) was the most potent inhibitor of glycoprotein-α (GP-α) and α-glucosidase. Its GP-α inhibitory activity (IC_{50} = 45.08 μM) was 10 times greater than that of the

Table 6 Isolated compounds from Australian tropical medicinal plants

Species	Part studied	Isolated compounds	References
Abutilon indicum (L.) Sweet	Leaves, whole plant	Methyl *trans-p*-coumarate; methyl caffeate; syringic acid; pinellic acid; abutilin; (R)-N-(1 '-methoxycarbonyl- 2 '-phenylethyl)-4-hydroxybenzamide; syringaldehyde; alantolactone; isoalantolactone	Khan et al. (2015), Kuo et al. (2008), Musthafa et al. (2021), Sharma and Ahmad (1989)
Acacia auriculiformis A.Cunn. ex Benth.	Heartwood, stem bark, funicles, leaves	(2S,3R,4R)-2-(3-Hydroxyphenyl)-4-methoxychromane-4,7,8-triol; (*E*)-3-(4-hydroxyphenyl)-1-(2,3,4-trihydroxyphenyl)prop-2-en-1-one; *trans*-2,3–3,4',7,8-tetrahydroxyflavanone; 3,4',7,8-tetrahydroxyflavone; teracacidin; (2R,3R,4R)-2-(3-hydroxyphenyl)-4-methoxychromane-4,7,8-triol; acaciaside A & B; α-spinasterol; botulin; *p*-propoxybenzoic acid	Lawal et al. (2020), Ahmadu et al. (2021), Prayogo et al. (2023), Mandal et al. (2005), Johnson et al. (2021)
Acalypha wilkesiana Müll.Arg.	Leaves; root and root bark	Gallic acid; corilagin; geraniin; rutin; kaempferol 3-*O*-rutinoside	Adesina et al. (2000)
Ageratum conyzoides L.	Leaves, stem, root, Whole plant	5,6,7,8,3,4,5-Heptamethoxyflavone; 5,6,7,8,3-pentamethoxy-4, 5-methylenedioxyflavone; coumarin; ageconyflavones A (5,6,7-trimethoxy-3′,4′-methylenedioxyflavone); ageconyflavones B (5,6,7,3′-tetramethoxy-4′-hydroxyflavone); ageconyflavones C (5,6,7,3′,5′-pentamethoxy-4′-hydroxyflavone); linderoflavone B; eupalestin; nobiletin; 5′-methoxynobiletin, 5,6,7,5′-tetramethoxy-3′,4′-methylenedioxyflavone; sinensetin; 5,6,7,8,3′-pentamethoxy-4′-hydroxyflavone and 5,6,7,8,3′,5′-hexamethoxy-4′-hydroxyflavone; 5,6,7,3',4',5'-hexamethoxyflavone; 5,6,7,8,3',4'-hexamethoxyflavone (nobiletin); 3',4'-methylenedioxy-5',5,6,7-tetramethoxyflavone; 5,6,7,8,5'-pentamethoxy-3',4'-methylenedioxyflavone	Moreira et al. (2007), Vyas and Mulchandani (1986), Binh et al. (2021)
Avicennia marina (Forssk.) Vierh.	Leaves and fruits, aerial	1,3-Benzodioxole,5,5-(tetrahydro-1H,3H-Furo[3,4-c]furan-1,4-diyl)bis-,[1 s-(1 alpha,3a alpha,4 beta,6a alpha)]; 11-hydroxy-8,11,13-abietatriene 12-O-beta-xylopyranoside; 6H alpha-11,12,16-trihydroxy-6,7-secoabieta-8,11,13-triene-6,7-dial 11,6-hemiacetal; 6H beta-11,12,16-trihydroxy-6,7-secoabieta-8,11,13-triene-6,7-dial 11,6-hemiacetal; (7'S*,8'R*)-4,4',9'-trihydroxy-3,3',5,5'-tetramethoxy-7,8-dehydro-9-al-2,7'-cyclolignan; 6,11,12,16-tetrahydroxy-5,8,11, 13-abitetetraen-7-one; lyoniresinol; lyoniresinol 9'-O-beta-D-glucopyranoside; diacetylmartynoside (Han et al. 2008); 2'-O-(5-phenyl-2E, 4E-pentadienoyl) mussaenosidic acid	Devi et al. (2014), Feng et al. (2006)
Brucea javanica (L.) Merr.	Seed	Brusatol; bruceantin; brucein A; bruceantinol; brucein B; 20-hydroxyyadanzigan; yadanzigan; bruceine F; bruceine E; javanicolides C & D; javanicosides B − F; yadanziolide A; bruceine D; javanicolides A & B; vanillic acid; bruceine E; *p*-hydroxybenzoic acid; luteolin; protocatechuic acid; gallic acid	Ryu et al. (2017), Yanzhi Zhan et al. (2020), Liu et al. (2012), Kim et al. (2004), Fukamiya et al. (1992), Kim et al. (2003), Abdulwali Ablat et al. (2017)

Table 6 continued

Species	Part studied	Isolated compounds	References
Cassytha filiformis L.	Whole plant	Precassythine; (+)-6S-ocotecine-N-oxide; isofiliformine; cassythic acid; cassythine; neolitsine; dicentrine; 1, 1,2-methylenedioxy-3,10,1-trimethoxyaporphine; (-)-O-methylflavinatine; (-)-salutaridine; isohamnetin-3-O-β-glucoside; isohamnetin-3-O-rutinoside	Huang et al. (2022), Tsai et al. (2008)
Castanospermum australe A.Cunn. & C.Fraser	Leaves, stem, wood	1-Epialexine; 2β,23-dihydroxy-3-O-(4-deoxy-β-l-threo-hex-4-enopyranosiduronic acid)-olean-12-en- 28-oic acid dimethyl ester; medicagenic acid 3-O-β-d-glucoside dimethyl ester; castanospermine (1,6,7,8-tetrahydroxy-octahydroindolizidine; koparin (7,3',4'-trihydroxy-2'-methoxyisoflavone or 7,2',3'-trihydroxy-4'-methoxyisoflavone); 7-Deoxy-6-epi-castanospermine; berberin; 6-epi-castanospermine; 3-epi-australine (3,7a-di-epi;-alexine); 1-epi-australine	Jones et al. (2010), Uddin Ahmad et al. (1992), Campbell et al. (1987), Berry et al. (1977), Sudhanshu Kumar Bharti et al. (2012), Molyneux et al. (1990b)
Cleome viscosa L.	Whole plant	Cembrenoid diterpene; malabaric acid; stigmast-4-en-3-one; stigmast-4-ene-3,6-dione; allantoin; atropine; nevirapine; gallic acid; caffeic acid; vanillic acid; kaempferitrin; lactam nonanoic acid (LNA) [2-amino-9-(4-oxoazetidin-2-yl)-nonanoic acid; cleomiscosins A-C; imperatorin	Dissanayake et al. (2022), Lakshmanan et al. (2019), Sharma and Shrivastav (2022), Jana and Biswas (2011), Meena et al. (2011), Lakshmanan et al. (2024)
Clerodendrum inerme Gaertn.	Leaves, stem, aerial, flower	Inermes A & B; 14,15-dihydro-15 beta-methoxy-3-epicaryoptin; 14,15-dihydro-15-hydroxy-3-epicaryoptin; icariol A; syringaresinol-4-O-beta-glucopyranoside; lariciresinol-4-O-beta-D-glucopyranoside; dehydrodiconiferyl alcohol-4-O-beta-D-glucopyranoside; leonuriside A; sammangaosides A, B and C; 3-hydroxy-3',4'-dimethoxychalcone; 3,2'-dihydroxy-3',4'-dimethoxychalcone; 7-O-methylwogonin; eucalyptin; crolerodendrum B; and other compounds as reported in Chan et al. (2023)	Pandey et al. (2005), Minh and Thuong (2021), Kanchanapoom et al. (2001), Shahabuddin et al. (2013), Ba Vinh et al. (2018), Chan et al. (2023)
Dodonaea viscosa Jacq.	Aerial part, leaves	Dodovisnoids A-G; 3,5,7,3′,4′-pentahydroxyflavone; hautriwaic acid; clerodane diterpenoids 1 and 2; 13,14-dihydroxy-15,16 dimethoxy-(-)-6a-hydroxy-5a,8a,9a,10a-cleroda-3-en-18-oic acid 1; (-)-6a-hydroxy-5a, 8a,9a,10a-cleroda-3,13-dien-16,15-olid-18-oic acid 2, 1-L-O-methyl-2-acetyl-3-*p-cis*-coumaryl-myo-inositol; methyl dodovisate A; methyl dodovisate B; 5,7,4'-trihydroxy-3',5'-di(3-methylbut-2-enyl)-3,6-dimethoxyflavone and 5,7,4'-trihydroxy-3'-(4-hydroxy-3-methylbutyl)-5'-(3-methylbut-2-enyl)-3,6-dimethoxyflavone; dodonic acid; hautriwaic acid; hautriwaic lactone; (+)-hardwickiic acid; 5-hydroxy-1,2-dehydro-5,10-dihydroprintzianic acid methyl ester; strictic acid; dodonolide; aliarin; 2,18-dihydroxylabda-7,13(*E*)-dien-15-oic acid; 5,7-dihydroxy-3,6,4'-trimethoxy-3'-(4-hydroxy-3-methyl-but-2-enyl)flavone	Zhang et al. (2016), Hamed Al Bimani and Hossain (2020), Mostafa et al. (2014), Niu et al. (2010), Wabo et al. (2012)

Table 6 continued

Species	Part studied	Isolated compounds	References
Eleocharis dulcis (Burm.f.) Trin. ex Hensch.	Whole plants, peels	Hexacosanoic acid; 5 alpha-stigmastane-3,6-dione; beta-sitosterol; stigmasterol; betulin; and tricin; orcinol glucoside; leonuriside A; 2-hydroxymethyl-6-(5-hydroxy-2-methyl-phenoxy-methyl)-tetra-hydro-pyran-3,4,5-triol; 1,4-dihydroxy-3-methoxy-phenyl-4-O-beta-D-glucopyranoside; 4',5'-dimethoxy-6,6-dimethylpyranoisoflavone; 3-methoxy-4-hydroxylonchocarpin; 4-hydroxylonchocarpin; 4-methoxylonchocarpin; barbigerone; lonchocarpusone; 6a,12a-dehydrodeguelin; 13-homo-13-oxa-6a, 12a-dehydrodeguelin and deguelin	Miles et al. (1994), Nie et al. (2019), Li et al. (2023)
Ficus racemosa L.	Bark	Lupeol; beta-sitosterol; (rel)-4,6-dihydroxy-5-[3-methyl-(*E*)-propenoic acid-3-yl]-7-beta-glucopyranosyl-(2alpha,3beta-dihydrobenzofuran}-(3,2:b)-[4alpha,5beta-dihydroxy-6alpha-hydroxymethyltetrahydropyran](racemosic acid); α-amyrin acetate	Bopage et al. (2018), Li et al. (2004), Narender et al. (2009)
Grewia hirsuta Vahl.	Leaves	(4*Z*, 12*Z*)-Cyclopentadeca-4, 12-dienone	Abirami and Natarajan (2014)
Heliotropium indicum L.	Leaves, root, whole plant	Helindicine; lycopsamine; (*E*)-ethyl-12- cyclohexyl-4,5-dihydroxydodec-2-enoate	Souza et al. (2005), López-Lorenzo et al. (2022)
Hibiscus vitifolius L.	Root, flower	Vitiquinolone, β-Amyrin acetate; n-octacosanol; β-amyrin; stigmasterol; xanthyletin; alloxanthoxyletin; xanthoxyletin; betulinic acid; methyl 27-caffeoyloxyoleanolate; oleanolic acid; kaempferol; quercetin; β-sitosterol-3-O-β-D-glucopyranoside; kaempferol-3-O-α-D-rhamnopyranoside; gossypin; quercetin-3-O-β-D-glucopyranoside; mangiferin; gossypin	Ramasamy and Saraswathy (2014), Ramasamy and Saraswathy (2013), Venkatesan and Sorimuthu Pillai (2012)
Macaranga tanarius Müll.Arg.	Fruit, leaves	Mallotinic acid; corilagin; chebulagic; macatannins A and B; nymphaeol A (6-geranyl eriodictyol); nymphaeol B (2′-geranyl eriodictyol); nymphaeol C (6-dimethylallyl-2′-geranyl eriodictyol), isonymphaeol B (5′-geranyl eriodictyol); 3′-geranyl naringenin; macatanarin D, schweinfurthin H; vedelianin; schweinfurthin F; schweinfurthin E; 4′deprenyl-mappain; schweinfurthins K-Q; vedelianin; schwenfurthins E–G; mappain; methyl-mappain; epoxynymphaeol C; (+)-pinoresinol 4-O-[6 ''-O-galloyl]-beta-D-glucopyranoside; macarangiosides E and F; tanarifuranonol; tanariflavanone C; tanariflavanone D; solophenol D	Gunawan-Puteri and Kawabata (2010), Natsume et al. (2021), Marliana et al. (2018), Yoshimura et al. (2017), Syah and Ghisalberti (2015), Doan et al. (2019), Péresse et al. (2017), Syah and Ghisalberti (2015), Matsunami et al. (2009), Phommart et al. (2005), Marliana et al. (2018)
Melastoma affine D.Don	Leaves, flower	Auranamide; patriscabratine; α-amyrin; quercitrin; quercetin; kaempferol-3-O-(2aEuro(3),6aEuro(3)-di-O-*p-trans*-coumaroyl)-beta-glucoside; naringenin; kaempferol; kaempferol-3-O-D-glucoside, kaempferol-3-O-(2", 6"-di-O-*p-trans*-coumaroyl) glucoside and kaempferol-3-O-D-glucoside	Sirat et al. (2010), Susanti et al. (2007)
Merremia tridentata (L.) Hallier f.	Stem, root	Apigenin; cosmosin; quercitrin; cymaroside	Vo Van et al. (2022)

Table 6 continued

Species	Part studied	Isolated compounds	References
Morinda citrifolia L.	Fruit, stem	*trans*-(3)E-3-(3,4-dihydroxybenzylidene)-5-(3,4- dihydroxyphenyl)-4-(hydroxymethyl)dihydrofuran-2(3H)-one; (−)-3,4,3′,4′-tetrahydroxy-9,7′β-epoxylignano-7β,9′-lactone; (7R,8R)-3-methoxy-1′-carboxy-4′,7-epoxy-8,3′-oxyneolignan-4,9-diol; (+)-3,4,3′,4′-tetrahydroxy-9,7′α-epoxylignano-7α,9′-lactone; (7R,8R)- 3,4,9-trihydroxy-4′,7-epoxy-8,3′-oxyneolignan-1′-al; (7′*E*),(7R,8S)-3,4,9-trihydroxy-4′,7-epoxy-8,3′-oxyneolignan-7′-en-8′-oic acid; ursolic acid; episesamin 2,6-dicatechol; (−)-3,3′-bisdemethylpinoresinol, (−)-pinoresinol; lirioresinol B; lirioresinol B dimethyl ether; americanin A; arteminorin D; rel-(7α,8β)-3-methoxy-4′,7-epoxy8,3′-oxyneolignan-4,9,9′-triol; americanoic acid A; methyl 3-(2,4-dihydroxy-5-methoxyphenyl)propionate; butyl 3-(2,4-dihydroxy-5-methoxyphenyl)propionate; 5-hydroxyhexyl 2-hydroxypropanoate; morindicinone (= 2-hydroxy-1,8-dimethoxy-7-methoxymethylanthraquinone); morindicininone (= 4-hydroxymethyl-1,3-dimethoxyanthraquinone); 2-hydroxyanthraquinone; 2-methoxyanthraquinone; asperulosidic acid; rutin; nonioside A; (2*E*,4*E*,7*Z*)-deca-2,4,7-trienoate-2-O-β-D-glucopyranosyl-β-D-glucopyranoside; tricetin	Nguyen et al. (2013), Wang et al. (2011), Siddiqui et al. (2006), Lee et al. (2020)
Ocimum gratissimum L.	Leaves	l-Caftaric acid; l-chicoric acid; eugenyl-β-D-glucopyranoside; vicenin-2; oleanolic acid; ursolic acid; acetate of oleanolic acid; pomolic acid; tormentic acid; xanthomicrol; β-sitosterol; stigmasterol	Casanova et al. (2014), Nganteng et al. (2022)
Ocimum tenuiflorum L.	Leaves	2-(4-Hydroxy-3-methoxyphenyl)-8-methoxy-6-prop-2-enyl-3,4-dihydro-2H-chromen-3-ol; dehydrodieugenol B	Ranteh et al. (2024), Dandekar et al. (2021)
Pandanus tectorius Parkinson	Fruit, leaves, aerial root	(*Z*)-4-Hydroxy-3-(4-hydroxy-3-methylbut-2-en-1-yl) benzaldehyde; *p*-hydroxybenzaldehyde; syringaldehyde; (*E*)-ferulaldehyde; (*E*)-sinapinaldehyde; vanillin and 5-hydroxymethylfurfual; pandanusin A; bergapten; 6-(6′-hydroxy-3′,7′-dimethylocta-2′,7′-dienyl)-7-hydroxycoumarin); 6-(6′,7′-dihydroxy-3′,7′-dimethyloct-2′-enyl)-7-hydroxycoumarin); (+)-syringaresinol; (+)-pinoresinol, (+)-lyoniresinol; (+)-medioresinol; (−)-balanophonin; luteolin, (*S*)-2,3-dihydroluteolin; 2,3-bis-(4-hydroxy-3-methoxyphenyl)-3-methoxypropanol; tachioside; *p*-hydroxycinamaldehyde; 1-O-(28-hydroxyoctacosanoyl)glycerol; methyl β-D-fructopyranoside; (8S, 8′S)-2,2’,3,3’-tetramethoxy-4’-hydroxy-epoxylignan-4-O-β-D-glucoside; 2,20,3,30-tetramethoxy-40-hydroxy-epoxylignan-4-Ob-D-glucoside; vomifoliol; threo-3,30-dimethoxy-4,80-oxyneoligna-9,40,70,90 -tetraol-7(8)-ene1; (7S, 8R)-4,7,9,90-tetrahydroxy-3,30-dimethoxy-8-O-40-neolignan; (þ)-isolariciresinol; 4,40-dimethoxy-30-hydroxy-7,90,70,9-diepoxylignan-3-O-b-D-glucopyranoside; (þ)-syringaresinol-O-b-D-glucopyranoside; (7R, 8R)-4,7,9,90-tetrahydroxy-3,30-dimethoxy-8-O-40-neolignan, secroisolariciresinol; 2-methoxy-4-methylphenyl 1-O-rutinoside; 3,5-dimethoxy-4-hydroxyphenyl 1-O-rutinoside and (S)-2-hydroxy-2-phenylethyl 1-O-rutinoside; 2-methoxy-4-hydroxymethylphenyl 1-O-rutinoside; cuneataside D; benzyl rutinoside;	Mai et al. (2015), Nguyen et al. (2016), Zhu and Zhang (2022), Sahakitpichan et al. (2020)

Table 6 continued

Species	Part studied	Isolated compounds	References
		2-phenethyl rutinoside; viridoside; 7,8-threo-7-methoxysyringylglycerol; 7,8-erythro-7-methoxysyringylglycerol; methyl caffeate; 3,5-di-O-caffeoyl-quinic acid 1-methyl ether; 4,5-di-O-caffeoyl-quinic acid 1-methyl ether; 3,4-di-O-caffeoyl-epi-quinic acid methyl ester; hedyotol D 7"-O-β-D-glucopyranoside	
Syzygium cumini (L.) Skeels	Leaves, bark, seed	Syzygioate A and B; dipropyl succinate; dioctyl phthalate; friedelin; mycaminose; N-{1-azabicyclo[2.2.2]octan-3-yl}-2-(6,7-dimethoxy-2-methyl-4-oxo-3,4-dihydroquinazolin-3-yl)acetamide; 6-amino-2-({1-[2-amino-3-(1H-indol-3-yl)propanoyl]pyrrolidin-2-yl}formamido)hexanoic acid; (2,2,6,6-tetramethylpiperidin-4-yl) 12-hydroxyoctadecanoate; 2-(docosanoylamino)-3-methylbutanoic acid; 4-carbamoyl-2-dodecylhexadecanoic acid; maslinic acid; 5-(hydroxymethyl) furfural; gallic acid; valoneic acid dilactone; rubuphenol; ellagic acid; flavopiridol; kaempferol; quercetin 3-O-α-L-rhamnopyranosiderhamnopyronside; kaempferol 3-O-β-Dglucuronopyranoside; myricetin 3-O-β-D-glucuronopyranoside; mearnsetin 3-O-(4″-O-acetyl)- α-L-rhamnopyranoside; lupeol; 7-hydroxycalamenene, gallic acid; syzygioate A and B; dipropyl succinate; dioctyl phthalate	Mujawah et al. (2023), Ghosh et al. (2024), Sawant et al. (2015), Aung et al. (2020), Sahab et al. (2023)
Terminalia catappa L.	Stem bark, leaves, fruit	3,4,5-Trimethoxyphenyl-1-O-(4-sulfo)-beta-D-glucopyranoside; chebuloside arjunoglucoside II; arjunolic acid; 3-betulinic acid; sitosterol-3–O-beta-D-glucopyranoside	Pertuit et al. (2015)
Ziziphus oenoplia (L.) Mill.	Root	Ziziphine N-Q	Suksamrarn et al. (2005)

standard GP-α inhibitor caffeine (IC_{50} = 457.34 μM), and its α-glucosidase inhibitory activity (IC_{50} = 26.41 μM) was 5.5 times greater than that of standard drug acarbose (IC_{50} = 145.83 μM) (Abdulwali Ablat et al. 2017). The compounds isolated from *Pandanus tectorus*, namely, (*Z*)-4-hydroxy-3-(4-hydroxy-3-methylbut-2-en-1-yl) benzaldehyde (**2**), *p*-hydroxybenzaldehyde (**3**), syringaldehyde (**4**) (*E*)-ferulaldehyde (**5**), (*E*)-sinapinaldehyde (**6**), vanillin (**7**) and 5-hydroxymethylfurfual (**8**), showed better α-glucosidase inhibitory activity (IC_{50} values ranging from 36.5 to 192.4 μM) than acarbose (IC_{50} = 214.5 μM) (Mai et al. 2015). Isolated compounds from the fruit of *Macaranga tanarius* were investigated for their mode of action on immortalised rat skeletal (L6) myoblast cell line. The L6 myoblast cell line is frequently utilised in vitro diabetic model system as due to its ability to differentiate into multinucleated myotubes and express proteins such as GLUT4. Isonymphaeol B (**15**) and 3′-geranyl naringenin (**16**) dose-dependently increased glucose uptake. These results suggest that compounds (**15**) and (**16**) positively affect glucose metabolism through the AMPK and GLUT1 pathways (Fig. 7) (Natsume et al. 2021).

Viscosol (**9**) from *Dodonaea viscosa*, improved insulin secretion and insulin resistance in high-fat diet (HFD)- and low-dose streptozotocin (STZ)-induced T2D mouse models (Table 4) (Sohail et al. 2022). Chicoric acid (**10**) (3 mg/kg bw), isolated from *Ocimum gratisimum*, also significantly decreased the blood glucose levels of diabetic mice by 53% at 120 min after treatment (Table 4) (Casanova et al. 2014). Alpha-amyrin acetate (**11**) (100 mg/kg bw), which was isolated from the fruits of *F. racemosa,* reduced blood glucose levels by 18.4% and 17.0% at 5 and 24 h, respectively, in a sucrose-challenged STZ-induced diabetic rat model (Narender et al. 2009; Mujawah et al. 2023).

Two compounds isolated from the seed extract of *Syzigium cumini,* mycaminose (**12**) and cuminoside (**13**) (50 mg/kg bw each), were evaluated for their antidiabetic properties in STZ-induced diabetic rats. Both compounds were able to significantly reduce blood glucose levels ($p < 0.05$) (Kumar et al. 2008). Additionally, these compounds significantly decreased the levels of triglyceride, low-density lipoprotein (LDL), cholesterol, and hepatic enzymes such as lactate dehydrogenase (LDH), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) in diabetic rats, while there was increased in high-density lipoprotein (HDL) level (Farswana et al. 2009). Gossypin (**14**), isolated from *Hibiscus vitifolius*, enhanced glucose tolerance and significantly normalised blood glucose, plasma insulin, and HbA1c levels after oral treatment in diabetic rats (Venkatesan and Sorimuthu Pillai 2012). Additionally, gossypin also increased glycogen levels and normalised blood urea and plasma protein levels. The efficacy of gossypin was comparable to that of a standard antidiabetic drug gliclazide (Venkatesan and Sorimuthu Pillai 2012).

Strategies for the biodiscovery of antidiabetic molecules

1. Techniques for the isolation and characterisation of antidiabetic compounds

The antidiabetic compounds from medicinal plants are obtained through bioassay-guided isolation techniques, as illustrated in Fig. 8. The plant materials were dried and powdered before extraction and fractionation. Polar solvents such as methanol, water, and ethanol (with various concentrations ranging from 50 to 96%) are commonly used for extraction, followed by fractionation with solvents of different polarities: *n*-hexane or petroleum ether (nonpolar), chloroform, or ethyl acetate (semipolar) and butanol (polar) (Laxman Sawant et al. 2015; Parasuraman et al. 2015; Masoongnoen et al. 2022). The most bioactive extracts or fractions identified via high-throughput in vitro screening, including cytotoxicity and antidiabetic assays, are selected for further isolation and characterisation of pure small molecules.

Isolation techniques use either Sephadex column chromatography (CC) with gradient elution from less polar to polar solvents or reverse-phase high-performance liquid chromatography (RP-HPLC), the most widely used HPLC method, where the stationary phase is less polar than the eluting solvent (Laxman Sawant et al. 2015; Ablat et al. 2017; Susanti et al. 2024). The purity of isolated compounds is confirmed using analytical high-performance liquid chromatography (HPLC) or conventional thin-layer chromatography (TLC). The approximate mass (*m*/*z*) of the isolated compounds are determined via liquid chromatography-mass spectrometry (LC-MS). Advanced high-

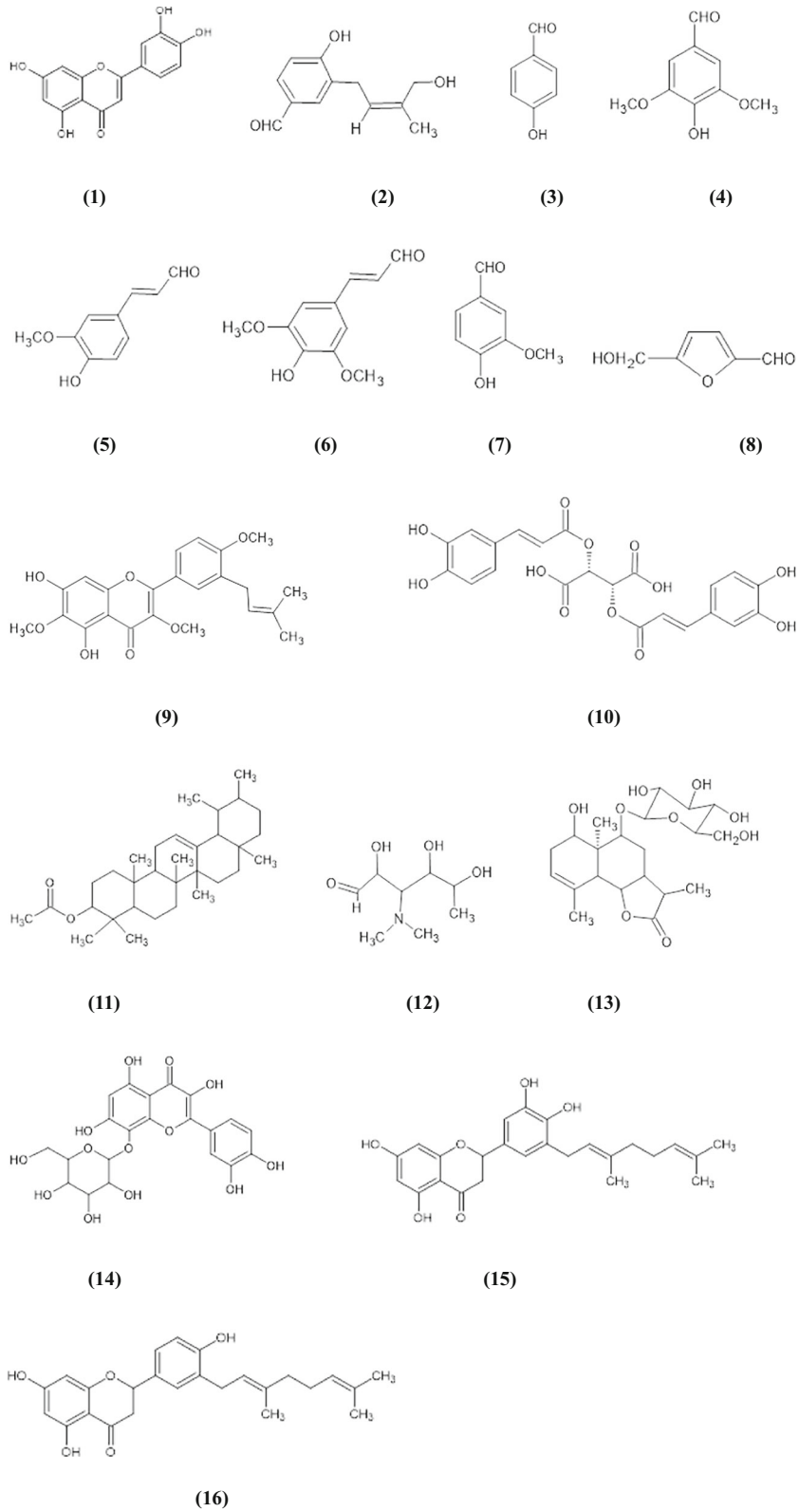

Fig. 7 Chemical structures of antidiabetic lead compounds identified via in vitro assays (**1**–**8**) and in vivo experimental animal models (**9**–**16**). Structures were drawn via ChemSketch ADC/Labs software

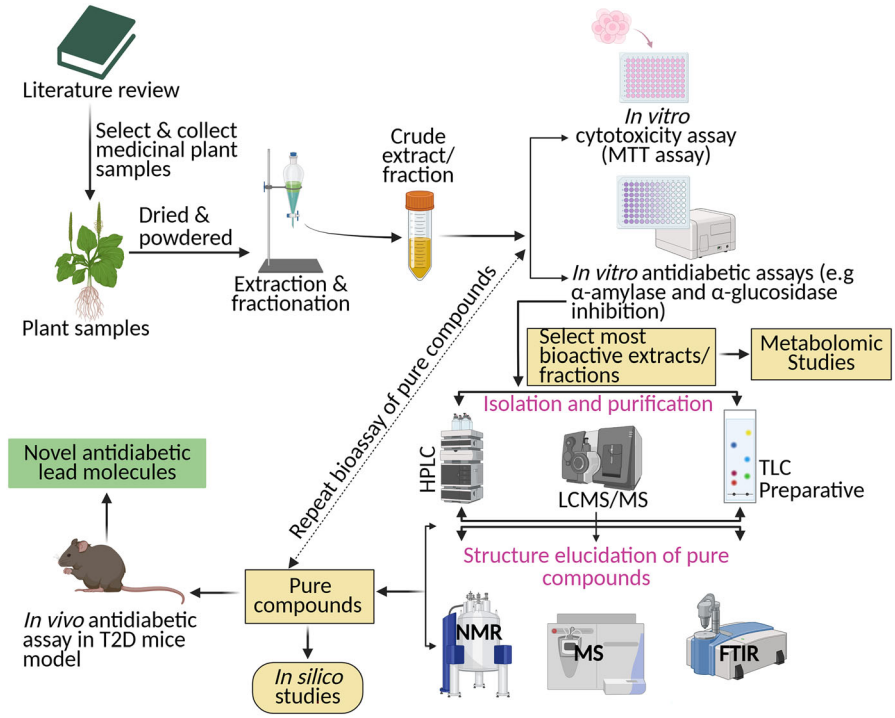

Fig. 8 Bioassay-guided isolation of novel antidiabetic lead molecules (Kabubii et al. 2024; Phukhatmuen et al. 2020)

resolution mass spectrometry (HRMS) enables the determination of the exact mass (*m*/*z*) of an isolated compound as a new natural product (Abirami Natarajan et al. 2015). Nuclear magnetic resonance (NMR) spectroscopy, including 1D NMR (^{1}H and ^{13}C NMR) and various 2D NMR experiments (HSQC, HMBC, NOESY, and TOCSY) are used to derive spectroscopic data to elucidate the chemical structure of isolated compounds (Dong et al. 2024). The antidiabetic properties of isolated and identified compounds are evaluated using appropriate in vitro assays and/or in vivo model systems to identify antidiabetic lead molecules.

2. Approaches for screening crude extracts or isolated compounds for their antidiabetic properties

From this literature review, three approaches were used for screening antidiabetic properties, namely, in vitro, in vivo, and in silico, to discover antidiabetic lead molecules from medicinal plants. In in vitro screening assays, the effects of test compounds on metabolic enzymes, especially α-amylase and α-glucosidase, were compared with those of standard compounds, such as acarbose (Hayaza et al. 2019, Vo Van et al. 2022). These enzymes are the key enzymes linked to T2D and play important roles in glucose production and carbohydrate digestion processes. The inhibition of these enzymes has become an important strategy in blood glucose management (Oboh et al. 2014; Hamden et al. 2013).

Diabetic animal models such as mice, rats, and rabbits were commonly used in in vivo testing. Diabetic condition was induced with a high-fat diet feeds or chemically using alloxan, streptozotocin, nicotinamide, or a combination of two or more inducers before the treatment. The hypoglycemic effect was then assessed by measuring the diabetic parameters such as decrease in fasting blood glucose levels, hemoglobin A1c (HbA1c), or glucose tolerance with reference to standard drugs such as glibenclamide and metformin. Other parameters assessed are pancreas histology and insulin level, triglycerides, low- and high-density lipoprotein (LDL and HDL), cholesterol, and hepatic enzymes. In addition to in vitro and in vivo methods, in silico method was also used to study the antidiabetic activities of compounds through molecular docking and binding affinities to specific

proteins. For example, 7-deoxy-6-epi-castanospermine, isolated from *Castanospermum australe* seeds, was a strong DPP-IV inhibitor comparable to berberine (Sudhanshu Kumar Bharti et al. 2012). Docking studies have shown that (4Z, 12Z)-cyclopentadeca-4,12-dienone, isolated from the leaves of *Grewia hirsuta,* effectively targets various diabetes-related sites (Abirami Natarajan et al. 2015; Abirami and Natarajan 2014).

Conclusion and future directions

In summary, this review identified 126 species of Australian tropical medicinal plants used by Australian Aboriginal people as folk medicines to treat wounds and diabetes-related conditions. These plants (126 species) belong to 47 families and 88 genera, of which Myrtaceae was the dominant family. The plant lifeforms were mostly shrubs, and the leaves were the most used plant parts. Among the 126 species, 28 were edible, and fruits were the most consumed by Aboriginal people. Crude plant extracts from 29 species have been tested for their antidiabetic properties through in vitro and/or in vivo assays to scientifically validate their ethnopharmacological uses. Among those species, crude extracts of *Syzygium cumini*, and *Morinda citrifolia* were the most widely studied for their antidiabetic activities. Furthermore, *Morinda citrifolia* extract and a combination of *Eleocharis dulcis* and *Brassica rapa* have been tested clinically in diabetic patients. A total of 374 compounds have been isolated from 26 species, of which 51 have been tested in vitro and/or in vivo for their antidiabetic properties. As a result, 16 compounds were identified as promising antidiabetic drug leads.

Australian tropical medicinal plants offer a natural and sustainable source of antidiabetic compounds, which have long been utilised in traditional treatments for diabetes-related conditions and hold a significant cultural importance for Indigenous communities. These plants are rich in diverse phytochemicals with potential health benefits, presenting promising opportunities for diabetes management through the development of drugs and nutraceuticals. However, limited research on many of these plants poses a challenge to their acceptance in mainstream medicine. Additionally, variability in plant extracts can lead to inconsistent study results, making it difficult to obtain approval for new treatments derived from these plants.

There are many challenges in utilising medicinal plants directly for antidiabetic treatments. Ensuring the consistent quality and potency of plant extracts and conducting rigorous clinical trials to validate their efficacy and safety are the main hurdles. It is also essential to identify lead antidiabetic compounds in these bioactive plant extracts, investigate their mechanisms of action and compare their efficacy with that of conventional antidiabetic drugs. Ethical considerations must be addressed by respecting the intellectual property and traditional knowledge of indigenous communities to foster collaboration among researchers, traditional healers, and indigenous communities. Advanced techniques such as genomics and metabolomics can be also employed to gain a deeper understanding of the bioactive compounds in these plants. Integrating these medicinal plants, including their crude extracts and purified compounds into clinical practice will require well-designed clinical trials and regulatory approval.

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Declaration

Competing interest All authors declare no competing interest.

References

Abirami N, Natarajan B (2014) Isolation and characterization of (4Z, 12Z)-cyclopentadeca-4, 12- dienone from indian medicinal plant Grewia hirsuta and its hyperglycemic effect on 3t3 and l6 cell lines. Int J Pharm Phytochem Res 6(2):393–398

Ablat A, Halabi MF, Mohamad J, Hasnan MH, Hazni H, Teh SH, Shilpi JA, Mohamed Z, Awang K (2017) Antidiabetic effects of Brucea javanica seeds in type 2 diabetic rats. BMC Complem Altern Med 17(1):94

Abushanab D, Liew D, Al-Badriyeh D, Marquina C, Ademi Z (2022) EPH79 projections of future health and economic burden of cardiovascular disease among patients with type 2 diabetes Mellitus in Australia. Estimates up to 2030. Value Health 25(7):S449

Adamu BF, Gao J, Jhatial AK, Kumelachew DM (2021) A review of medicinal plant-based bioactive electrospun nano fibrous wound dressings. Mater des 209:109942

Adesina SK, Idowu O, Ogundaini AO, Oladimeji H, Olugbade TA, Onawunmi GO, Pais M (2000) Antimicrobial constituents of the leaves of *Acalypha wilkesiana* and *Aacalypha hispida*. Phytother Res 14(5):371–374

Adisakwattana S, Pudhom K, Yibchok-anun S (2009) Influence of the methanolic extract from Abutilon indicum leaves in normal and streptozotocin-induced diabetic rats. Afr J Biotech 8:2011–2015

Agunbiade OS, Afolabi OB, Jaiyesimi KF, Adewale OB, Okoh PO, Adewole E, Mabayoje SO, Agboola EK (2024) Antioxidant capacities, antidiabetic potentials, and mineral compositions of pap aqua and aqueous extracts from *Ocimum gratissimum* L. J HerbMed Pharm 13(1):43–51

Agunbiade OS, Ojezele OM, Ojezele JO, Ajayi AY (2012) Hypoglycaemic activity of Commelina africana and *Ageratum conyzoides* in relation to their mineral composition. Afr Health Sci 12(2):198–203

Ahmadu AA, Delehouzé C, Haruna A, Mustapha L, Lawal BA, Udobre A, Baratte B, Triscornia C, Autret A, Robert T, Bulinski JC, Rousselot M, Simoes Eugénio M, Dimanche-Boitrel M-T, Petzer JP, Legoabe LJ, Bach S (2021) Betulin, a newly characterized compound in Acacia auriculiformis Bark, is a multi-target protein kinase inhibitor. Molecules (Basel, Switzerland) 26(15):4599

Ahmed F, Urooj A (2010) In vitro studies on the hypoglycemic potential of *Ficus racemosa* stem bark. J Sci Food Agric 90(3):397–401

AIHW (2024) Diabetes: Australian facts https://www.aihw.gov.au/reports/diabetes/diabetes/contents/summary Accessed 25 May 2024

Akhtar MS, Ahmed M, Gulzar K, Adnan H (2011) Hypoglycemic activity of *Dodonaea viscosa* leaves in normal and alloxan-induced diabetic rabbits. Diabetol Croat 40(3):71–79

ALA (2024) Atlas of living Australia, Open access to Australia's biodiversity data

Algenstaedt P, Stumpenhagen A, Westendorf J (2018) The effect of *Morinda citrifolia* L. fruit juice on the blood sugar level and other serum parameters in patients with diabetes type 2. Evid-Based Complem Altern Med 2018:3565427–3565510

Ali MA, Wahed MII, Khatune NA, Rahman BM, Barman KR, Islam MR (2015) Antidiabetic and antioxidant activities of ethanolic extract of *Semecarpus anacardium* (Linn.) bark. BMC Complem Altern Med 15(1):96

Ali MK, Pearson-Stuttard J, Selvin E, Gregg EW (2022) Interpreting global trends in type 2 diabetes complications and mortality. Diabetologia 65(1):3–13

Amelia F, Parbuntari H, Iryani S (2024) Phytoconstituents of *Terminalia catappa* linn fruits extract exhibit promising antidiabetic activities against α-amylase and α-glucosidase in vitro and in silico. Inf Med Unlocked 47:101509

APC (2024) Vascular plants Australian plant census (APC)

Arif A, Gillani SR, Hussain H (2022) Eleocharis dulcis individually and in combination with *Brassica rapa* as a best cure of diabetes with zero side effects. J Food Process Preserv 46(9):536

Armenia N, Alen Y, Ismed F, Yuliandra Y, Ananda R (2016) Blood sugar lowering effectiveness of *Cassytha filiformis* fractions on diabetic mice. Res J Pharm Biol Chem Sci 7(6):1142–1147

Arulselvan P, Ghofar HAA, Karthivashan G, Halim MFA, Ghafar MSA, Fakurazi S (2014) Antidiabetic therapeutics from natural source: a systematic review. Biomed Prev Nutr 4(4):607–617

Arunachalam K, Parimelazhagan T (2012) Antidiabetic activity of aqueous root extract of *Merremia tridentata* (L.) Hall. f. in streptozotocin–induced–diabetic rats. Asian Pac J Trop Med 5(3):175–179

Atawodi SE, Adepoju OA, Nzelibe HC (2017) Antihyperglycaemic and hypolipidemic effect of methanol extracts of *Ageratum conyzoides* L. (Asteraceae) in normal and diabetic rats. Trop J Pharm Res 16(5):989

Aung EE, Kristanti AN, Aminah NS, Takaya Y, Ramadhan R (2020) Plant description, phytochemical constituents and bioactivities of *Syzygium* genus: a review. Open Chem 18(1):1256–1281

AVH (2024) The Australasian virtual herbarium

Ba Vinh L, Nguyet TM (2018) A new rearranged abietane diterpene from *Clerodendrum inerme* with antioxidant and cytotoxic activities. Nat Prod Res 32(17):2001–2007

Baehaki A, Widiastuti I, Lestari S, Masruro M, Putra HA (2021) Antidiabetic and anticancer activity of Chinese water chestnut (*Eleocharis dulcis*) extract with multistage extraction. J Adv Pharm Technol Res 12(1):40–44

Balamurugan K, Nishanthini A, Mohan VR (2014) Antidiabetic and antihyperlipidaemic activity of ethanol extract of *Melastoma malabathricum* Linn. leaf in alloxan induced diabetic rats. Asian Pac J Trop Biomed 4(Suppl 1):S442–S448

Barr A, Chapmann J, Smith N, Wightman G, Knight T, Mills L, Andrews M, Alexander V (1993) Traditional aboriginal

medicines in the northern territory of Australia. Conservation Commission of the Northern Territory, Darwin
Barry AR (2018) Patients' perceptions and use of natural health products. Can Pharm J 151(4):254–262
Bassalat N, Kadan S, Melamed S, Yaron T, Tietel Z, Karam D, Kmail A, Masalha M, Zaid H (2023) In vivo and in vitro antidiabetic efficacy of aqueous and methanolic extracts of orthosiphon *Stamineus Benth*. Pharmaceutics 15(3):945
Berry RC, Eade RA, Simes JJH (1977) Extractives of Australian timbers. XVII. The isolation, structure and synthesis of koparin (7,2',3'-Trihydroxy-4'-methoxyisoflavone). Aust J Chem 30(8):1827–1835
Bharat Bhushan BB, Satish Sardana SS, Gulshan Bansal GB (2015) Anti-diabetic potentials of *Clerodendrum inerme*, *Jasminum mesyni* Hance and *Callistemon citrinus* on nicotinamide-streptozotocin induced type 2 diabetic rats. Int J Phytomed 7(2):136–141
Bharathy P, Thanikachalam PV (2024) Harnessing traditional herbal medicine: molecular insights into diabetic wound healing for modern therapeutics. Dig Chin Med 7(4):388–404
Bharti SK, Krishnan S, Kumar A, Rajak KK, Murari K, Bharti BK, Gupta AK (2012) Antihyperglycemic activity with DPP-IV inhibition of alkaloids from seed extract of *Castanospermum australe*: investigation by experimental validation and molecular docking. Phytomedicine 20(1):24–31
Bhaskara Rao R, Murugesan T, Sinha S, Saha BP, Pal M, Mandal SC (2002) Glucose lowering efficacy of Ficus racemosa bark extract in normal and alloxan diabetic rats. Phytother Res 16(6):590–592
Bindon P (1996) Useful bush plants. Western Australian Museum, London
Binh TD, Kusunoki R, Nguyen TQC, Nakagami A, Kanaori K, Nguyen YDH, Pham TLA, Nguyen CC, Vang LV, Kamei K (2021) Identification and structural characterization of anti-endoplasmic reticulum stress compounds from *Ageratum conyzoides* (L.). Rec Nat Prod 15(2):82–90
Bopage NS, Gunaherath KB (2018) Dual function of active constituents from bark of *Ficus racemosa* L. in wound healing. BMC Complem Altern Med 18(1):29–29
Brem H, Tomic-Canic M (2007) Cellular and molecular basis of wound healing in diabetes. J Clin Investig 117(5):1219–1222
Campbell BC, Molyneux RJ, Jones KC (1987) Differential inhibition by castanospermine of various insect disaccharidases. J Chem Ecol 13(7):1759–1770
Casanova LM, da Silva D, Sola-Penna M, de Magalhães Camargo LM, de Moura Celestrini D, Tinoco LW, Costa SS (2014) Identification of chicoric acid as a hypoglycemic agent from Ocimum gratissimum leaf extract in a biomonitoring in vivo study. Fitoterapia 93:132–141
Chan EWC, Wong SK, Chan HT (2023) Volkameria inermis: an overview of its chemical constituents and pharmacological properties, notably the amelioration of motor tics. J Herbmed Pharmacol 12(2):176–186
Chatterjee SMD, Khunti KP, Davies MJP (2017) Type 2 diabetes. The Lancet (British Edition) 389(10085):2239–2251
Chen H, Wu Z, Chen D, Huang F, Chen H, Wu Z, Chen D, Huang F (2024) Correlation between blood glucose level and poor wound healing after posterior lumbar interbody fusion in patients with type 2 diabetes. Int Wound J 21(1):56
Clarke PA (2007) Aboriginal people and their plants. Rosenberg Publishing Pty Ltd, New South Wales
Cribb AB, Cribb JW (1981) Wild medicine in Australia. Collins Publications, Sydney
Dandekar PD, Kotmale AS, Chavan SR, Kadlag PP, Sawant SV, Dhavale DD, RaviKumar A (2021) Insights into the inhibition mechanism of human pancreatic α-amylase, a type 2 diabetes target, by dehydrodieugenol B isolated from *Ocimum tenuiflorum*. ACS Omega 6(3):1780–1786
DeFelice SL (1995) The nutraceutical revolution: its impact on food industry R&D. Trends Food Sci Technol 6(2):59–61
Demling RH (2009) Nutrition, anabolism, and the wound healing process: an overview. Eplasty 9:e9–e9
Devi AS, Rajkumar J, Beenish TK (2014) Detection of antibacterial compound of *Avicennia marina* against pathogens isolated from urinary tract infected patients. Asian J Chem 26(2):458–460
DiabetesAustralia (2024) Type 2 diabetes, https://www.diabetesaustralia.com.au/about-diabetes/type-2-diabetes/
Dira M (2022) Phytochemical screening and antidiabetic activities test of ethanol extract from *Syzygium cumini* L. seeds in male Wistar rats induced by alloxan. Pharm Educ 22:165–168
Dissanayake AA, Georges K, Nair MG (2022) Cyclooxygenase enzyme and lipid peroxidation inhibitory terpenoids and steroidal compounds as major constituents in cleome viscosa leaves. Planta Med 88(14):1287–1292
Doan TMH, Nguyen TL, Trinh TTV, Vu VN, Phi TD, Litaudon M, Roussi F, Chau VM, Pham VC (2019) Cytotoxic phenolic compounds from fruit glandular trichomes of *Macaranga tanarius*. J Anal Methods Chem 2019:2917032–2917035
Dong S-H, Duan Z-K, Bai M, Huang X-X, Song S-J (2024) Advanced technologies targeting isolation and characterization of natural products. TrAC Trends Anal Chem 175:117711
Dubey R, Prabhakar PK, Gupta J, Dubey R, Prabhakar PK, Gupta J (2022) Epigenetics: key to improve delayed wound healing in type 2 diabetes. Mol Cell Biochem 477(2):371–383
Edgar J, Gilbert M, Edgar D, Edgar T, Howard M, Dann G, Gilbert S, Boxer B, Sampi P (1997) Mayi some of bush fruits of the West Kimberley. Magabala Books Aboriginal Corporation, London
El-Manawaty MA, Gohar L (2018) In vitro alpha-glucosidase inhibitory activity of Egyptian plant extracts as an indication for their antidiabetic activity. Asian J Pharm Clin Res 11(7):360–367
Eming SA, Murray PJ, Pearce EJ (2021) Metabolic orchestration of the wound healing response. Cell Metab 33(9):1726–1743
Falanga V (2005) Wound healing and its impairment in the diabetic foot. Lancet 366:1736–1743
Farswana M, Mazumder P, Parcha V (2009) 'Modulatory effect of an isolated compound from *Syzygium cumini* seeds on biochemical parameters of diabetes in rats. Int J Green Pharm 3:485

Feng Y, Li XM, Duan XJ, Wang BG (2006) A new acylated iridoid glucoside from *Avicennia marina*. Chin Chem Lett 17(9):1201–1204

Fern K (2014) Useful tropical plants database

Florentin M, Kostapanos MS, Papazafiropoulou AK (2022) Role of dipeptidyl peptidase 4 inhibitors in the new era of antidiabetic treatment. World J Diabetes 13(2):85–96

Fukamiya N, Okano M, Miyamoto M, Tagahara K, Lee K-H (1992) Antitumor agents, 127. Bruceoside C, a new cytotoxic Quassinoid Glucoside, and related compounds from *Brucea javanica*. J Nat Prod 55(4):468–475

Gajera HP, Gevariya SN, Hirpara DG, Patel SV, Golakiya BA (2017) Antidiabetic and antioxidant functionality associated with phenolic constituents from fruit parts of indigenous black jamun (*Syzygium cumini* L.) landraces. J Food Sci Technol 54(10):3180–3191

Galicia-Garcia U, Benito-Vicente A, Jebari S, Larrea-Sebal A, Siddiqi H, Uribe KB, Ostolaza H, Martín C (2020) Pathophysiology of type 2 diabetes *Mellitus*. Int J Mol Sci 21(17):6275

Ghosh AK, Panda SK, Hu HB, Schoofs L, Luyten W (2024) Compounds isolation from Syzygium cumini leaf extract against the Vibrio species in shrimp through bioassay-guided fractionation. Nat Prod Res 11:638

Goyal PK, Jeyabalan G (2021) Hypoglycemic and anti-lipidemic evaluation of fruit extract and solvent fractions of *Ziziphus oenoplia* in streptozotocin-induced diabetic rats. Int J Pharm Sci Nanotechnol 14(4):5549–5556

Gross CL (1993) The breeding system and pollinators of Melastoma affine (Melastomataceae): a pioneer shrub in tropical Australia. Biotropica 25(4):468–474

Gulati V, Gulati P, Harding IH, Palombo EA (2015) Exploring the anti-diabetic potential of Australian Aboriginal and Indian Ayurvedic plant extracts using cell-based assays. BMC Complem Altern Med 15(1):8–8

Gunawan-Puteri MDPT, Kawabata J (2010) Novel α-glucosidase inhibitors from Macaranga tanarius leaves. Food Chem 123(2):384–389

Hamden K, Mnafgui K, Amri Z, Aloulou A, Elfeki A (2013) Inhibition of key digestive enzymes related to diabetes and hyperlipidemia and protection of liver-kidney functions by trigonelline in diabetic rats. Sci Pharm 81(1):233–246

Bimani HA (2020) A new antimicrobial compound from the leaves of Dodonaea viscosa for infectious diseases. Bioactive Mater 5(3):602–610

Han L, Huang X, Dahse HM, Moellmann U, Grabley S, Lin W, Sattler I (2008) New abietane diterpenoids from the mangrove *Avicennia marina*. Planta Med 74(4):432–437

Han X, Tao Y, Deng Y, Yu J, Sun Y, Jiang G (2017) Metformin accelerates wound healing in type 2 diabetic db/db mice. Mol Med Rep 16(6):8691–8698

Hardstaff LK, Sommerville KD, Funnekotter B, Bunn E, Offord CA, Mancera RL (2022) Myrtaceae in Australia: use of cryobiotechnologies for the conservation of a significant plant family under threat. Plants (Basel) 11(8):1017

Hayaza S, Istiqomah S, Kuncoroningrat Susilo RJ, Inayatillah B, Ansori ANM, Winarni D, Husen SA, Darmanto W (2019) Antidiabetic activity of Ketapang (*Terminalia catappa* L.) leaves extract in streptozotocin-induced diabetic mice. Indian Vet J 96(12):11–13

Henning RJ (2018) Type-2 diabetes mellitus and cardiovascular disease. Fut Cardiol 14(6):491–509

Hsu Y-C, Chang C-C, Hsieh C-C, Shih Y-H, Chang H-C, Lin C-L (2023) Therapeutic potential of extracts from *Macaranga tanarius* (MTE) in diabetic nephropathy. Plants (Basel) 12(3):656

Huang P-K, Lin S-R, Chang C-H, Tsai M-J, Lee D-N, Weng C-F (2019) Natural phenolic compounds potentiate hypoglycemia via inhibition of *Dipeptidyl peptidase* IV. Sci Rep 9(1):15585–15611

Huang Z, Cao M, Wang R, Zhang Y, Zhang X, Dong L, Zhang C (2022) Two new aporphine alkaloids with glucose consumption increasing activity from *Cassytha filiformis*. Phytochem Lett 51:23–27

IDF (2021) Diabetes Atlas the 10th edition, https://diabetesatlas.org/idfawp/resourcefiles/2021/07/IDF_Atlas_10th_Edition_2021.pdf

Iheagwam FN, Iheagwam OT, Onuoha MK, Ogunlana OO, Chinedu SN (2022) Terminalia catappa aqueous leaf extract reverses insulin resistance, improves glucose transport and activates PI3K/AKT signalling in high fat/streptozotocin-induced diabetic rats. Sci Rep 12(1):10711–10711

Ikegami H, Babaya N, Noso S (2021) β-Cell failure in diabetes: common susceptibility and mechanisms shared between type 1 and type 2 diabetes. J Cutan Immunol Allergy 12(9):1526–1539

Im MJC, Hoopes JE (1970) Energy metabolism in healing skin wounds. J Surg Res 10(10):459–464

Izundegui DG, Nayor M (2022) Metabolomics of type 1 and type 2 diabetes: insights into risk prediction and mechanisms. Curr DiabRep 22(2):65–76

Jameson JL (2010) Harrison's endocrinology, 2nd edn. The McGraw-Hill Companies, London

Jana A, Biswas SM (2011) Lactam nonanic acid, a new substance from Cleome viscosa with allelopathic and antimicrobial properties. J Biosci 36(1):27–35

Jangra M, Sharma S, Kumar M (2011) Evaluation of antihyperglycemic activity of *Dodonaea viscosa* leaves in normal and STZ-diabetic rats. Int J Pharm Pharm Sci 3(SUPPL. 3):69–74

Jiang X, Hansen HCB, Strobel BW, Cedergreen N (1987) (2018) "What is the aquatic toxicity of saponin-rich plant extracts used as biopesticides?" Environ Pollut 236:416–424

Johnson EC, Ukpe RA, Etim EI, Umoh UF, Eseyin OA, Udoh AE, Mboho T, Anthony PC (2022) In vitro antidiabetic, aphrodisiac and antimicrobial properties of para-propoxybenzoic acid isolated from *Acacia auriculiformis* A. Cunn Ex. Benth (Fabaceae) stem bark. Trop J Pharm Res 20(3):613–620

Jones L, Hollinshead J, Fleet GWJ, Thompson AL, Watkin DJ, Gal ZA, Jenkinson SF, Kato A, Nash RJ (2010) Isolation of the pyrrolizidine alkaloid 1-epialexine from *Castanospermum australe*. Phytochem Lett 3(3):133–135

Joshi H, Vaishnav D, Sanghvi G, Rabadia S, Airao V, Sharma T, Parmar S, Sheth N (2016) Ficus recemosa bark extract attenuates diabetic complications and oxidative stress in STZ-induced diabetic rats. Pharm Biol 54(9):1586–1595

Jugran AK, Rawat S, Devkota HP, Bhatt ID, Rawal RS (2021) Diabetes and plant-derived natural products: from

ethnopharmacological approaches to their potential for modern drug discovery and development. Phytother Res 35(1):223–245
Kabubii ZN, Mbaria JM, Mathiu PM, Wanjohi JM, Nyaboga EN (2024) Bioassay guided isolation and compounds identification of the anti-diabetic fractions of (rosemary) Rosmarinus officinalis leaves extract. Clini Phytoscie 10(1):16–11
Kamaei L, Moghadamnia D (2021) Comparison of antidiabetic effects of aqueous extract of the leaves and fruits of avicennia marina in streptozotocin-induced diabetic male rats. Iran J Toxicol 13(2):7–12
Kanchanapoom T, Kasai R, Chumsri P, Hiraga Y, Yamasaki K (2001) Megastigmane and iridoid glucosides from *Clerodendrum inerme*. Phytochemistry (Oxford) 58(2):333–336
Karmakar UK, Paul A, Bokshi B (2021) Investigation of antidiarrheal, analgesic, antidiabetic and cytotoxic activities of the aerial parts of flagellaria indica (Flagellariaceae). Trop J Nat Prod Res 5(2):281–286
Khalfaoui T, Basora N, Ouertani-Meddeb A (2010) Apoptotic factors (Bcl-2 and Bax) and diabetic retinopathy in type 2 diabetes. J Mol Histol 41(2–3):143–152
Khan HBH, Vinayagam KS, Renny CM, Palanivelu S, Panchanadham S (2013) Potential antidiabetic effect of the Semecarpus anacardium in a type 2 diabetic rat model. Inflammopharmacology 21(1):47–53
Khan RS, Senthi M, Rao PC, Basha A, Alvala M, Tummuri D, Masubuti H, Fujimoto Y, Begum AS (2015) Cytotoxic constituents of *Abutilon indicum* leaves against U87MG human glioblastoma cells. Nat Prod Res 29(11):1069–1073
Khil J, Kim SM, Chang J, Choi S, Lee G, Son JS, Park SM, Keum N (2023) Changes in total cholesterol level and cardiovascular disease risk among type 2 diabetes patients. Sci Rep 13(1):8342–8342
Kim IH, Suzuki R, Hitotsuyanagi Y, Takeya K (2003) Three novel quassinoids, javanicolides A and B, and javanicoside A, from seeds of *Brucea javanica*. Tetrahedron 59(50):9985–9989
Kim IH, Takashima S, Hitotsuyanagi Y, Hasuda T, Takeya K (2004) New Quassinoids, Javanicolides C and D and Javanicosides B−F, from Seeds of *Brucea javanica*. J Nat Prod 67(5):863–868
Krisanapun C, Lee SH, Peungvicha P, Temsiririrkkul R, Baek SJ (2011) Antidiabetic activities of *Abutilon indicum* (L.) sweet are mediated by enhancement of adipocyte differentiation and activation of the GLUT1 promoter. Evid Based Complem Alternat Med 2:167684
Krisanapun C, Peungvicha P, Temsiririrkkul R, Wongkrajang Y (2009) Aqueous extract of Abutilon indicum Sweet inhibits glucose absorption and stimulates insulin secretion in rodents. Nutr Res 29(8):579–587
Kumar A, Raju I, Jayachandran T, Deecaraman M, Aravindan P, Padmanabhan N, Krishan M (2008) Anti-diabetic activity of *Syzygium cumini* and it's isolated compound against streptozotocin-induced diabetic rats. J Med Plants Res 2:246–249
Kuo P-C, Yang M-L, Wu P-L, Shih H-N, Thang TD, Dung NX, Wu T-S (2008) Chemical constituents from *Abutilon indicum*. J Asian Nat Prod Res 10(7):689–693
Kushwaha PS, Raj V, Singh AK, Keshari AK, Saraf SA, Mandal SC, Yadav RK, Saha S (2015) Antidiabetic effects of isolated sterols from *Ficus racemosa* leaves. RSC Adv 5(44):35230–35237
Kyriaziz S (1995) Bush medicine of the northern pennisula area of Cape York. Nai Beguta Agama Aboriginal Corporation, New York
Lavanya L (2022) Study of in vitro activity on glucose uptake of 3T3L1 cells, RIN5f cells, and glycemic index stimulation inhibitory effect of *Abutilon indicum* (L.) extract. Science 1:963
Lakshmanan G, Altemimi AB, Sivaraj C, Selvakumari J, Karthik L, Saravanan K, Viswanathan V, Pandian A, Cacciola F, Rashad Ali M, Najm MAA, Gamal Abedelmaksoud T (2024) Imperatorin from the aerial parts of *Cleome viscosa* L.: a characterization study and evaluation of the antibacterial activity. Nat Prod Res 38(5):848–858
Lakshmanan G, Sivaraj C, Ammar A, Anantha Krishnan D, Gopinath S, Saravanan K, Gunasekaran K, Murugesan K (2019) Isolation and structural elucidation of allantoin a bioactive compound from *Cleome viscosa* L.: a combined experimental and computational investigation. Pharm J 11(6):1391–1400
Lassak EV, McCarthy T (2011) Australian medicinal plants: a complete guide to identification and usage. New Holland Publishers, Australia
Lawal BA, Udobre A, Elufioye TO, Ahmadu AA, Olanipekun B (2020) Novel cholinesterase inhibitory effect of α-spinasterol isolated from the leaves of *Acacia auriculiformis* A. CUNN Ex. Benth (Fabaceae). Trop J Pharm Res 19(7):1473–1479
Lawrie SAM (2023) Bush foods–an aussie culinary experience
Lee D, Yu JS, Huang P, Qader M, Manavalan A, Wu X, Kim J-C, Pang C, Cao S, Kang KS, Kim KH (2020) Identification of anti-inflammatory compounds from Hawaiian Noni (*Morinda citrifolia* L.) Fruit Juice. Molecules (Basel, Switzerland) 25(21):4968
Lee SY, Park SL, Hwang JT, Yi SH, Nam YD, Lim SI (2012) Antidiabetic effect of Morinda citrifolia (Noni) fermented by Cheonggukjang in KK-A(y) Diabetic Mice. Evid Based Complem Altern Med 2012:163280
Lega IC, Lipscombe LL (2020) Review: diabetes, obesity, and cancer—pathophysiology and clinical implications. Endocr Rev 41(1):33–52
Li J, Kang Z, Yu H, Feng Y, Zhang X, Zhao Y, Dong L, Zhang L, Dong J, Li Y, Ma S (2023) Potent insecticidal activity of *Eleocharis dulcis* (Burm. f.) Trin peel extract and its main components against aphids. Pest Manag Sci 79(4):1295–1304
Li RW, Leach DN, Myers SP, Lin GLD, Leach GJ, Waterman PG (2004) A new anti-inflammatory glucoside from *Ficus racemosa* L. Planta Med 70(5):421–426
Lin B, Qi X, Fang L, Zhao L, Zhang R, Jing J, Zhang S, Yang X, Hou Z, Xue P (2021) In vivo acute toxicity and mutagenic analysis of crude saponins from Chenopodium quinoa Willd husks. RSC Adv 11(8):4829–4841
Lin Q-R, Jia L-Q, Lei M, Gao D, Zhang N, Sha L, Liu X-H, Liu Y-D (2024) Natural products as pharmacological modulators of mitochondrial dysfunctions for the treatment of diabetes and its complications: an update since 2010. Pharmacol Res 200:107054–107054
Litwiniuk A, Bik W, Kalisz M, Baranowska-Bik A (2021) Inflammasome NLRP3 potentially links obesity-associated

low-grade systemic inflammation and insulin resistance with Alzheimer's disease. Int J Mol Sci 22(11):5603

Liu J-H, Zhao N, Zhang G-J, Yu S-S, Wu L-J, Qu J, Ma S-G, Chen X-G, Zhang T-Q, Bai J, Chen H, Fang Z-F, Zhao F, Tang W-B (2012) Bioactive Quassinoids from the seeds of *Brucea javanica*. J Nat Prod 75(4):683–688

Lolok N, Sumiwi SA, Sahidin I, Levita J (2023) Stigmasterol isolated from the ethyl acetate fraction of Morinda citrifolia fruit (using the bioactivity-guided method) inhibits α-amylase activity: In vitro and in vivoanalyses. World Acad Sci J 5(5):639

López-Lorenzo Y, Sánchez-Mendoza ME, Arrieta-Baez D, Perez-Ruiz AG, Arrieta J (2022) Gastroprotective activity of (E)-ethyl-12-cyclohexyl-4,5-dihydroxydodec-2-enoate, a compound isolated from Heliotropium indicum: role of nitric oxide, prostaglandins, and sulfhydryls in its mechanism of action. Pharm Biol 60(1):1207–1213

Low T (1989) Wild food plants of Australia. Angus and Robertson, Melbourne

Low T (1990) Bush medicine: a pharmacopoeia of natural remedies. Angus and Robertson, Melbourne

Ly HT, Nguyen TTH, Tran TTL, Lam BT, Phung TTH, Le VM (2019) Hypoglycemic and antioxidant activities of Clerodendrum inerme leaf extract on streptozotocin-induced diabetic models in mice. Chin Herbal Med 11(4):387–393

Mahadeva Rao US, Subramanian S (2009) Biochemical evaluation of antihyperglycemic and antioxidative effects of *Morinda citrifolia* fruit extract studied in streptozotocin-induced diabetic rats. Med Chem Res 18(6):433–446

Mahindrakar KV, Rathod VK (2022) Ultrasound-assisted intensified aqueous extraction of phenolics from waste *Syzygium cumini* leaves: kinetic studies and evaluation of antioxidant, antidiabetic and anticancer potential. Food Biosci 46:101547

Mahmood NA, Hassan MR, Ahmad S, Mohd Nawi H, Pang NTP, Rahim SA (2020) Nutraceutical use among patients with chronic disease attending outpatient clinics in a tertiary hospital. Evid-Based Complem Altern Med 2020:1–9

Mai DT, Le TD, Nguyen TP, Phan NM, Nguyen HA, Nguyen TTP, Tran LQ (2015) A new aldehyde compound from the fruit of Pandanus tectorius Parkinson ex Du Roi. Nat Prod Res 29(15):1437–1441

Maiden JH (1889) The useful native plants of Australia. Turner and Henderson, Sydney

Malik MN, Haq I-U, Fatima H, Ahmad M, Naz I, Mirza B, Kanwal N (2022) Bioprospecting *Dodonaea viscosa* Jacq.; a traditional medicinal plant for antioxidant, cytotoxic, antidiabetic and antimicrobial potential. Arab J Chem 15(3):103688

Mandal P, Sinha Babu SP, Mandal NC (2005) Antimicrobial activity of saponins from *Acacia auriculiformis*. Fitoterapia 76(5):462–465

Mapp E (1986) Gastrointestinal disorders in diabetes mellitus. Radiology 161(2):292–292

Marliana E, Hairani R, Tjahjandarie TS, Tanjung M (2018) Antiplasmodial activity of flavonoids from *Macaranga tanarius* leaves. Earth Environ Sci 144(1):12011

Masaenah E, Elya B, Setiawan H, Fadhilah Z, Wediasari F, Nugroho GA (2021) Antidiabetic activity and acute toxicity of combined extract of Andrographis paniculata, Syzygium cumini, and Caesalpinia sappan. Heliyon 7(12):e08561

Mashraqi MM, Chaturvedi N, Alam Q, Alshamrani S, Bahnass MM, Ahmad K, Alqosaibi AI, Alnamshan MM, Ahmad SS, Beg MMA, Mishra A, Shaikh S, Rizvi SMD (2021) Biocomputational prediction approach targeting FimH by natural SGLT2 inhibitors: a possible way to overcome the uropathogenic effect of SGLT2 inhibitor drugs. Molecules (Basel, Switzerland) 26(3):582

Masoongnoen J, Sansenya S, Tongpoolsomjit K, Viyoch J, Wechakorn K (2022) Antidiabetic, tyrosinase inhibitory, and free radical scavenging activities of the purified extracts from Morinda citrifolia unripe fruits. Songklanakarin J Sci Technol 44(3):735–743

Mathew S, Lee LS, Race D (2016) Conceptualising climate change adaption for native bush food production in arid Australia. Learn Commun 19:98–115

Matsunami K, Otsuka H, Kondo K, Shinzato T, Kawahata M, Yamaguchi K, Takeda Y (2009) Absolute configuration of (+)-pinoresinol 4- O-[6″- O-galloyl]- β- d-glucopyranoside, macarangiosides E, and F isolated from the leaves of Macaranga tanarius. Phytochemistry (Oxford) 70(10):1277–1285

Meena A, Yadav DK, Srivastava A, Khan F, Chanda D, Chattopadhyay SK (2011) In Silico exploration of anti-inflammatory activity of natural coumarinolignoids. Chem Biol Drug des 78(4):567–579

Miles DH, Tunsuwan K, Chittawong V, Hedin PA, Kokpol U (1994) Boll weevil antifeedants from *Eleocharis dulcis* Trin. J Agric Food Chem 42(7):1561–1562

Minh TT, Thuong NTM (2021) Lignans from the stems of Clerodendrum inerme Gaertn. Viet J Chem 59(2):187–191

Mohammad SA, Nabi SA, Marella S, Thandaiah KT, Jyothi Kumar MV, Rao CA (2014) Phytochemical screening and antihyperglycemic activity of Heliotropium indicum whole plant in Streptozotocin induced diabetic rats. J Appl Pharm Sci 4(12):065–071

Mohammed A, Yaro H (2007) Effects of aqueous leaves extract of *Ocimum gratissimum* on blood glucose levels of streptozocin-induced diabetic wistar rats. Afr J Biotech 6(18):2087–2090

Molyneux RJ, Tropea JE, Elbein AD (1990) 7-Deoxy-6-epicastanospermine, a trihydroxyindolizidine alkaloid glycosidase inhibitor from Castanospermum australe. J Nat Prod 53(3):609–614

Moreira MD, Picanço MC, Barbosa LCA, Guedes RNC, Barros EC, Campos MR (2007) Compounds from Ageratum conyzoides: isolation, structural elucidation and insecticidal activity. Pest Manag Sci 63(6):615–621

Mostafa AE, El-Hela AA, Mohammad A-EI, Jacob M, Cutler SJ, Ross SA (2014) New secondary metabolites from *Dodonaea viscosa*. Phytochem Lett 8:10–15

Mousavi L, Salleh RM, Murugaiyah V, Asmawi MZ (2016) Hypoglycemic and anti-hyperglycemic study of *Ocimum tenuiflorum* L. leaves extract in normal and streptozotocin-induced diabetic rats. Asian Pac J Trop Biomed 6(12):1029–1036

Mujawah A, Rauf A, Bawazeer S, Wadood A, Hemeg HA, Bawazeer S (2023) Isolation, structural elucidation, in vitro anti-α-glucosidase, anti-β-secretase, and in silico studies of

bioactive compound isolated from *Syzygium cumini* L. Processes 11(3):880

Muliasari H, Hamdin CD, Aulia N, Hariyati I, Ihsan M (2019) The proposed mechanism of action of *Brucea javanica* (L) Merr. seed in experimentally diabetic rats. American Institute of Physics Inc., London

Musthafa SA, Dabdoub W, Sadiq M, Munuswamy-Ramanujam G (2021) Syringaldehyde isolated from *Abutilon indicum* Linn. leaves exhibits broad spectrum anti-microbial activity. Elsevier, London, pp 335–339

Nagappa AN, Thakurdesai PA, Venkat Rao N, Singh J (2003) Antidiabetic activity of *Terminalia catappa* Linn. fruits. J Ethnopharmacol 88(1):45–50

Narender T, Khaliq T, Singh AB, Joshi MD, Mishra P, Chaturvedi JP, Srivastava AK, Maurya R, Agarwal SC (2009) Synthesis of α-amyrin derivatives and their in vivo anti-hyperglycemic activity. Eur J Med Chem 44(3):1215–1222

Natarajan A, Sugumar S, Bitragunta S, Balasubramanyan N (2015) Molecular docking studies of (4Z, 12Z)-cyclopentadeca-4, 12-dienone from Grewia hirsuta with some targets related to type 2 diabetes. BMC Complem Altern Med 15(1):73–73

Natsume N, Yonezawa T, Saito Y, Woo J-T, Teruya T (2021) Prenylflavonoids from fruit of *Macaranga tanarius* promote glucose uptake via AMPK activation in L6 myotubes. J Nat Med 75(4):813–823

Nganteng DND, Melong R, Mbiekop EP, Maffo T, Allémann É, Delie F, Wafo P, Tchaleu BN, Dzoyem JP (2022) Chemical constituents and cytotoxic activity of *Ocimum gratissimum* L. S Afr J Bot 150:330–333

Nguyen P-H, Yang J-L, Uddin MN, Park S-L, Lim S-I, Jung D-W, Williams DR, Oh W-K (2013) Protein tyrosine phosphatase 1B (PTP1B) inhibitors from Morinda citrifolia (Noni) and their insulin mimetic activity. J Nat Prod 76(11):2080–2087

Nguyen TP, Le TD, Minh PN, Dat BT, Pham NKT, Do TML, Nguyen DT, Mai TD (2016) A new dihydrofurocoumarin from the fruits of *Pandanus tectorius* Parkinson ex Du Roi. Nat Prod Res 30(21):2389–2395

Nie H, Huang S, Li X, Gong J, Wu F, Yin J, Liao Y, Wu S, Luo Y (2019) Identification of compounds from chufa (*Eleocharis dulcis*) peels with inhibitory acrylamide formation activity. Rev Bras 29(4):483–487

Niu H-M, Zeng D-Q, Long C-L, Peng Y-H, Wang Y-H, Luo J-F, Wang H-S, Shi Y-N, Tang G-H, Zhao F-W (2010) Clerodane diterpenoids and prenylated flavonoids from Dodonaea viscosa. J Asian Nat Prod Res 12(1):7–14

Nwaehujor C, Uwagie-Ero E, Clifford A, Igile G (2021) Anti-diabetic and anti-oxidant activities of the methanol extract and fractions of Cassytha filliformis Linn. Science 1:163–170

Oboh G, Isaac AT, Akinyemi AJ, Ajani RA (2014) Inhibition of key enzymes linked to type 2 diabetes and sodium nitroprusside induced lipid peroxidation in rats' pancreas by phenolic extracts of avocado pear leaves and fruit. Int J Biomed Sci 10(3):208–216

Odoh UE, Ndubuokwu RI, Inya-Agha SI, Osadebe PO, Uzor PF, Ezejiofor M (2014) Antidiabetic activity and phytochemical screening of *Acalypha wilkesiana* (Euphorbiaceae) Mull Arg. roots in alloxan-induced diabetic rats. Sci Res Essays 9(7):204–212

Oguntibeju OO (2019) Medicinal plants and their effects on diabetic wound healing. Veterinary World 12(5):653–663

Oyebode OA, Erukainure OL, Koorbanally NA, Islam MS (2018) Acalypha Wilkesiana "Java White": identification of some bioactive compounds by Gc-Ms and their effects on key enzymes linked to type 2 diabete. Acta Pharm 68(4):425–439

Pandey R, Verma RK, Gupta MM (2005) Neo-clerodane diterpenoids from *Clerodendrum inerme*. Phytochemistry (Oxford) 66(6):643–648

Parasuraman S, Balamurugan S, Christapher P, Petchi R, Yeng W, Sujithra J, Vijaya C (2015) Evaluation of antidiabetic and antihyperlipidemic effects of hydroalcoholic extract of leaves of *Ocimum tenuiflorum* (Lamiaceae) and prediction of biological activity of its phytoconstituents. Pharmacognosy Research 7(2):156–165

Patel S, Srivastava S, Singh MR, Singh D (2019) Mechanistic insight into diabetic wounds: pathogenesis, molecular targets and treatment strategies to pace wound healing. Biomed Pharmacother 112:108615

Péresse T, Jézéquel GL, Allard P-M, Pham V-C, Huong DTM, Blanchard F, Bignon JRM, Lévaique H (2017) Cytotoxic prenylated stilbenes isolated from *Macaranga tanarius*. J Nat Prod 80(10):2684–2691

Pertuit D, Mitaine-Offer A-C, Miyamoto T, Tanaka C, Delemasure S, Dutartre P, Lacaille-Dubois M-A (2015) A new aromatic compound from the stem bark of *Terminalia catappa*. Nat Prod Commun 10(6):1005–1007

Phommart S, Sutthivaiyakit P, Chimnoi N, Ruchirawat S, Sutthivaiyakit S (2005) Constituents of the leaves of *Macaranga tanarius*. J Nat Prod 68(6):927–930

Phukhatmuen P, Raksat A, Laphookhieo S, Charoensup R, Duangyod T, Maneerat W (2020) Bioassay-guided isolation and identification of antidiabetic compounds from Garcinia cowa leaf extract. Heliyon 6(4):e03625–e03625

Piragine E, Petri D, Giometto S, Martelli A, Lucenteforte E, Calderone V (2022) Potential effects of Alliaceae and Brassicaceae edible plants on blood glucose levels in patients with type 2 diabetes: a systematic review and meta-analysis of clinical trials. Pharmacol Res 185:106519–106519

Prayogo YH, Batubara I, Sari RK, Egra S, Yamauchi K, Mitsunaga T, Syafii W (2023) Chemical constituent of acacia auriculiformis wood extractives and their antioxidant activity. Jurnal Sylva Lestari (Online) 11(3):370–381

Rafe MR (2017) A review of five traditionally used anti-diabetic plants of Bangladesh and their pharmacological activities. Asian Pac J Trop Med 10(10):933–939

Ramasamy D, Saraswathy A (2013) Isolation of methyl 27-caffeoyloxyoleanolate-a new oleanane triterpenoid from the roots of hibiscus vitifolius. Nat Prod Commun 8(4):433–434

Ramasamy D, Saraswathy A (2014) Vitiquinolone-a quinolone alkaloid from *Hibiscus vitifolius* Linn. Food Chem 145:970–975

Rangra N, Samanta S, Pradhan K (2021) Evaluation of *Acacia auriculiformis* Benth. leaves for wound healing activity in type 2 diabetic rats. Pharmacogn Mag 17(6):129–142

Ranteh O, Tedasen A, Rahman MA, Ibrahim MA, Sama-ae I (2024) Bioactive compounds from *Ocimum tenuiflorum* and *Poria cocos*: a novel natural compound for insomnia

treatment based on a computational approach. Comput Biol Med 175:108491–108491

Rao BS, Reddy KE, Parveen K, Narendra BL, Shekhar SC, Mangala L (2014) Effects of Cleome viscosa on hyperalgesia, oxidative stress and lipid profile in STZ induced diabetic neuropathy in Wistar rats. Pak J Pharm Sci 27(5):1137–1145

Ryu SM, Kwon J, Seo YH, Song EG, Hong SS, Kim BS, Hong JS, Ryu KH, Lee D (2017) Quassinoids isolated from Brucea javanica inhibit pepper mottle virus in pepper. Virus Res 227:49–56

Sadoughi SD, Hosseini SM (2020) Effects of hydroalcoholic leaf extract of avicennia marina on apoptotic, inflammatory, oxidative stress, and lipid peroxidation indices and liver histology of type 1 diabetic rats. Hepatitis Month 20(4):485

Sahab N, Khan D, Ullah H, Kiran S, Khan S (2023) Two new cholinesterase inhibitory and antioxidative constituents from *Syzygium cumini*. Iran J Chem Chem Eng Int 42(4):1164–1171

Sahakitpichan P, Chimnoi N, Thamniyom W, Ruchirawat S, Kanchanapoom T (2020) Aromatic rutinosides from the aerial roots of *Pandanus tectorius*. Phytochem Lett 37:47–50

Sathya A, Siddhuraju P (2013) Protective effect of bark and empty pod extracts from Acacia auriculiformis against paracetamol intoxicated liver injury and alloxan induced type II diabetes. Food Chem Toxicol 56:162–170

Sawant L, Singh VK, Dethe S, Bhaskar A, Balachandran J, Mundkinajeddu D, Agarwal A (2015) Aldose reductase and protein tyrosine phosphatase 1B inhibitory active compounds from Syzygium cumini seeds. Pharm Biol 53(8):1176–1182

Scheen AJ (2020) Sodium-glucose cotransporter type 2 inhibitors for the treatment of type 2 diabetes mellitus. Nat Rev Endocrinol 16(10):556–577

Seetharam YN, Chalageri G, Setty SR (2002) Hypoglycemic activity of Abutilon indicum leaf extracts in rats. Fitoterapia 73(2):156–159

Shahabuddin SK, Munikishore R, Trimurtulu G, Gunasekar D, Deville A, Bodo B (2013) Two new chalcones from the flowers of clerodendrum inerme. Nat Prod Commun 8(4):459–460

Sharma H, Shrivastav A (2022) HPLC purification of bio-actives of cleome viscosa and their anticancer activity against breast cancer cell lines. Orient J Chem 38(6):1505–1513

Sharma PV, Ahmad ZA (1989) 2 Sesquiterpene lactones from abutilon-indicum. Phytochemistry 28(12):3525–3525

Shittu S-TT, Lasisi TJ, Shittu SA-S, Adeyemi A, Adeoye TJ, Alada AA (2021) Ocimum gratissimum enhances insulin sensitivity in male Wistar rats with dexamethasone-induced insulin resistance. J Diabetes Metab Disord 20(2):1257–1267

Siddiqui BS, Sattar FA, Begum S, Gulzar T, Ahmad F (2006) New anthraquinones from the stem of Morinda citrifolia Linn. Nat Prod Res 20(12):1136–1144

Silbernag S, Lang F, Gay RD, Rothenburger A (2016) Color atlas of pathophysiology. Thieme, Stuttgart

Simamora A, Santoso AW, Timotius KH (2019) α-Glucosidase inhibitory effect of fermented fruit juice of *Morinda Citrifolia* L. and combination effect with acarbose. Curr Res Nutr Food Sci 7(1):218–226

Sirat HM, Susanti D, Ahmad F, Takayama H, Kitajima M (2010) Amides, triterpene and flavonoids from the leaves of *Melastoma malabathricum* L. J Nat Med 64(4):492–495

Sohail A, Fayyaz H, Muneer H, Raza I, Ikram M, Uddin Z, Gul S, Almohaimeed HM, Alsharif I, Alaryani FS, Ullah I (2022) Targeted inhibition of protein tyrosine phosphatase 1B by viscosol ameliorates type 2 diabetes pathophysiology and histology in diabetic mouse model. BioMed Res Int 22:963

Sophia D, Manoharan S (2007) Hypolipidemic activities of *Ficus racemosa* Linn. bark in alloxan induced diabetic rats. Afr J Tradit Complement Altern Med 4(3):279–288

Souza JSN, Machado LL, Pessoa ODL, Braz-Filho R, Overk CR, Yao P, Cordell GA, Lemos TLG (2005) Pyrrolizidine alkaloids from Heliotropium indicum. J Braz Chem Soc 16(6):1410–1414

Spampinato SF, Caruso GI, De Pasquale R, Sortino MA, Merlo S (2020) The treatment of impaired wound healing in diabetes: looking among old drugs. Pharmaceuticals (Basel, Switzerland) 13(4):60

Stachura A, Khanna I, Wlodarski P, Stachura A, Khanna I, Krysiak P, Paskal W, Włodarski P (2022) Wound healing impairment in type 2 diabetes model of leptin-deficient mice—a mechanistic systematic review. Int J Mol Sci 23(15):8621

Subramaniam S, Hedayathullah Khan HB, Gomathy G, Palanvelu S, Tiruvaiyaru Panchanadham S (2014) Effect of semecaprus anacardium on diabetes-induced alterations in the activities of marker enzymes and antioxidant enzymes in type 2 diabetes induced cardiac vascular damage model in rats. J Diet Suppl 11(4):347–360

Suksamrarn S, Suwannapoch N, Aunchai N, Kuno M, Ratananukul P, Haritakun R, Jansakul C, Ruchirawat S (2005) Ziziphine N, O, P and Q, new antiplasmodial cyclopeptide alkaloids from Ziziphus oenoplia var. brunoniana. Tetrahedron 61(5):1175–1180

Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, Stein C, Basit A, Chan JCN, Mbanya JC, Pavkov ME, Ramachandaran A, Wild SH, James S, Herman WH, Zhang P, Bommer C, Kuo S, Boyko EJ, Magliano DJ (2022) IDF Diabetes Atlas: global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Res Clin Pract 183:109119–109119

Suresh Y, Rajasekar G, Lavanya T, Lakshminarsimhulu B, Reddy KS, Reddy SR (2020) Antioxidant and antidiabetic properties of isolated fractions from methanolic extract derived from the whole plant of *Cleome viscosa* L. Fut J Pharm Sci 6(1):1–18

Susanti D, Sirat HM, Ahmad F, Ali RM, Aimi N, Kitajima M (2007) Antioxidant and cytotoxic flavonoids from the flowers of *Melastoma malabathricum* L. Food Chem 103(3):710–716

Susanti I, Pratiwi R, Rosandi Y, Hasanah AN (2024) Separation methods of phenolic compounds from plant extract as antioxidant agents candidate. Plants 13(7):965

Swain SK, Dash UC, Kanhar S, Sahoo AK (2024) Network pharmacology-based elucidation of bioactive compounds and experimental exploration of antidiabetic mechanisms of Hydrolea zeylanica. Cell Signal 114:96

Syah YM, Ghisalberti EL (2015) Flavanone derivatives from Macaranga tanarius. Biochem Syst Ecol 62:151–154

Syama HP, Arun KB, Sinumol G, Dhanya R, Suseela Anusree S, Nisha P, Ravi Shankar L, Sundaresan A, Jayamurthy P (2018) Syzygium cumini seed exhibits antidiabetic potential via multiple pathways involving inhibition of α-glucosidase, DPP-IV, glycation, and ameliorating glucose uptake in L6 cell lines. J Food Process Preserv 42(2):e13464

Tan SY, Mei Wong JL, Sim YJ, Wong SS, Mohamed Elhassan SA, Tan SH, Ling Lim GP, Rong Tay NW, Annan NC, Bhattamisra SK, Candasamy M (2019) Type 1 and 2 diabetes mellitus: a review on current treatment approach and gene therapy as potential intervention. Diabetes Metab Syndr 13(1):364–372

Thiyagarajan G, Muthukumaran P, Prabhu D, Balasubramanyam M, Baddireddi LS (2024) ameliorates high fat diet induced glucose intolerance, insulin resistance, weight gain, hepatic injury and nephrotoxicity through modulation of PTP1B and PPARγ signaling. Environ Toxicol 39(3):1086–1098

Tropea JE, Molyneux RJ, Kaushal GP, Pan YT, Mitchell M, Elbein AD (1989) Australine, a pyrrolizidine alkaloid that inhibits amyloglucosidase and glycoprotein processing. Biochemistry (Easton) 28(5):2027–2034

Tsai TH, Wang GJ, Lin LC (2008) Vasorelaxing alkaloids and flavonoids from Cassytha filiformis. J Nat Prod 71(2):289–291

Turpin G, Ritmejerytė E, Jamie J, Crayn D, Wangchuk P (2022) Aboriginal medicinal plants of Queensland: ethnopharmacological uses, species diversity, and biodiscovery pathways. J Ethnobiol Ethnomed 18(1):1–54

Uddin Ahmad V, Ahmed W, Usmanghani K (1992) Triterpenoid saponins from leaves of Castanospermum australe. Phytochemistry 31(8):2805–2807

UTP (2024) The useful tropical plants database

Veerapur VP, Prabhakar KR, Parihar VK, Bansal P, Srinivasan KK, Priyadarsini KI, Unnikrishnan MK (2010) Antidiabetic, hypolipidaemic and antioxidant activity of Dodonaea viscosa aerial parts in streptozotocin-induced diabetic rats. Int J Phytomed 2(1):59–70

Venkatesan T, Sorimuthu Pillai S (2012) Antidiabetic activity of gossypin, a pentahydroxyflavone glucoside, in streptozotocin-induced experimental diabetes in rats. J Diabetes 4(1):41–46

Van Vo L, Pham EC, Nguyen CV, Duong NTN, Vi Le Thi T, Truong TN (2022) In vitro and in vivo antidiabetic activity, isolation of flavonoids, and in silico molecular docking of stem extract of *Merremia tridentata* (L.). Biomed Pharmacother 146:112611–112611

Vyas AV, Mulchandani NB (1986) Polyoxygenated flavones from Ageratum conyzoides. Phytochemistry (Oxford) 25(11):2625–2627

Wabo HK, Chabert P, Tane P, Noté O, Tala MF, Peluso J, Muller C, Kikuchi H, Oshima Y, Lobstein A (2012) Labdane-type diterpenes and flavones from Dodonaea viscosa. Fitoterapia 83(5):859–863

Wang G, He Q-W, Feng T, Liu J-K (2011) Two new phenylpropanoids and one propanoate from Morinda citrifolia. J Asian Nat Prod Res 13(3):238–241

Wasana KGP, Attanayake AP, Jayatilaka KAPW, Weerarathna TP (2021) Antidiabetic activity of widely used medicinal plants in the Sri Lankan traditional healthcare system: new insight to medicinal flora in Sri Lanka. Evid-Based Complem Altern Med 2021:6644004–6644012

Webb LJ (1959) Some new records of medicinal plants used by the aborigines of tropical Queensland and New Guinea, vol 71. Royal Society of Queensland, Brisbane

WFO (2024) The World Flora Online (WFO) Plant list

Wharton S, Davies M, Dicker D, Lingvay I, Mosenzon O, Rubino DM, Pedersen SD (2022) Managing the gastrointestinal side effects of GLP-1 receptor agonists in obesity: recommendations for clinical practice. Postgrad Med 134(1):14–19

WHO (2024) 'World Health Organization: Diabetes', [online], https://www.who.int/health-topics/diabetes#tab=tab_1. Accessed May 27

Williams C (2010) Medicinal plants in Australia, Bush medicine, vol 1. Rosenberg Publishing Pty Ltd., Kenthurst

Williams CJ (2021) Phytochemistry of Australia's tropical rainforest: medicinal potential of ancient plants, 1st edn. CSIRO PUBLISHING, Collingwood

Wilson C (2010) Diabetes Dapagliflozin: an insulin-independent, therapeutic option for type 2 diabetes mellitus. Nat Rev Endocrinol 6(10):531–531

Wu C, Zhang X, Zhang X, Luan H, Sun G, Sun X, Wang X, Guo P, Xu X (2014) The caffeoylquinic acid-rich Pandanus tectorius fruit extract increases insulin sensitivity and regulates hepatic glucose and lipid metabolism in diabetic db/db mice. J Nutr Biochem 25(4):412–419

Xu L, Li Y, Dai Y, Peng J (2018) Natural products for the treatment of type 2 diabetes mellitus: pharmacology and mechanisms. Pharmacol Res 130:451–465

Yadav JP, Verma A, Pathak P, Dwivedi AR, Singh AK, Kumar P, Khalilullah H, Jaremko M, Emwas A-H, Patel DK (2024) Phytoconstituents as modulators of NF-κB signalling: investigating therapeutic potential for diabetic wound healing. Biomed Pharmacother 177:117058

Yoshimura K, Hosoya T, Fujinami M, Ohta T, Kumazawa S (2017) Nymphaeol-C, a prenylflavonoid from Macaranga tanarius, suppresses the expression of fibroblast growth factor 18. Phytomedicine (Stuttgart) 36:238–242

Zhan Y, Tan T, Qian K, Yang S, Feng Y, Wen Q (2020) Quassinoids from seeds of Brucea Javanica and their anticomplement activities. Nat Prod Res 34(8):1186–1191

Zhang L-B, Liao H-B, Zhu H-Y, Yu M-H, Lei C, Hou A-J (2016) Antiviral clerodane diterpenoids from Dodonaea viscosa. Tetrahedron 72(49):8036–8041

Zheng S, Wang Y, Liu H, Chang W, Xu Y, Lin F (2019) Prediction of hemolytic toxicity for saponins by machine-learning methods. Chem Res Toxicol 32(6):1014–1026

Zhu R, Chen B, Bai Y, Miao T, Rui L, Zhang H, Xia B, Li Y, Gao S, Wang X-D, Zhang D (2020) Lycopene in protection against obesity and diabetes: a mechanistic review. Pharmacol Res 159:104966–104966

Zhu Z-Y, Zhang P-Z (2022) A new lignan from Pandanus tectorius. Nat Prod Res 36(21):5553–5558