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Medicinal Plants and Bioactive Compounds in the Management of Type 2 Diabetes Mellitus (Part I)

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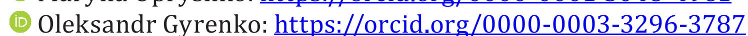
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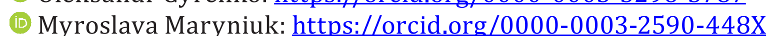
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Type 2 diabetes mellitus (T2DM) is a common metabolic disorder characterised by chronic hyperglycaemia, insulin resistance and progressive beta-cell dysfunction. It is often accompanied by dyslipidaemia, low-grade inflammation and an increased risk of cardiovascular disease. While pharmacological therapies are effective in controlling blood sugar levels, their long-term use may be limited due to variable efficacy, adverse effects and an inability to sufficiently prevent complications in certain patient groups. Consequently, there has been a growing focus on medicinal plants and dietary bioactive compounds as complementary strategies with multi-target metabolic actions. This review summarises the current evidence regarding the anti-hyperglycaemic potential of various medicinal plants, such as *Cinnamomum* spp., *Panax* spp., *Zingiber officinale*, *Allium sativum*, *Allium cepa*, *Aloe vera*, *Sesamum indicum*, *Azadirachta indica*, *Momordica charantia*, *Ocimum tenuiflorum* and *Curcuma longa*. The emphasis is on their phytochemical profiles, mechanisms of action, and findings from *in vitro*, *in vivo*, and clinical studies. The antidiabetic effects of these plants are mainly attributed to compounds such as polyphenols, flavonoids, saponins, and terpenoids, which modulate key metabolic pathways. Reported mechanisms include the inhibition of carbohydrate-digesting enzymes, the improvement of insulin secretion and sensitivity, the enhancement of glucose uptake (e.g. via the AMPK/GLUT4 pathways), and the reduction of oxidative stress and inflammation. Preclinical and clinical studies suggest that these plant-derived compounds may contribute to improved glycaemic control, including reductions in fasting glucose and HbA1c. However, clinical evidence remains inconsistent due to heterogeneity in study design, plant composition, dosage, and patient characteristics. Future research should prioritise the standardisation of formulations, rigorous clinical validation and the evaluation of long-term safety, in order to support the integration of these compounds into evidence-based diabetes management.

Keywords: Type 2 diabetes mellitus, phytotherapy, medicinal plants, antioxidant activity, α-glucosidase inhibition

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Introduction

Diabetes mellitus (DM) is one of the most significant challenges facing modern medicine. Its prevalence is rising worldwide, imposing a substantial burden on healthcare systems. According to the International Diabetes Federation (IDF, 2021), 537 million adults were living with diabetes globally in 2021, and this figure is expected to rise to 783 million by 2045. Around 90% of cases are type 2 diabetes mellitus (T2DM), which is linked to insulin resistance, obesity, a sedentary lifestyle and poor dietary habits (Olokoba et al., 2012; Wang et al., 2020). DM has been shown to markedly reduce quality of life by increasing the risk of stroke, myocardial infarction, renal failure, blindness and limb amputations, ultimately contributing to premature mortality (Młynarska et al., 2025). Furthermore, the growing global burden of diabetes underscores the urgent necessity for preventive and management strategies that transcend conventional treatment approaches.

According to the International Diabetes Federation (IDF, 2021), 537 million adults worldwide were living with diabetes in 2021. This figure is projected to rise to 643 million by 2030 and 783 million by 2045. Between 2013 and 2018, the prevalence among adults increased from 10.95 to 12.4%. The main contributing factors are unhealthy diets, physical inactivity, smoking, alcohol consumption and obesity. Impaired beta-cell function combined with obesity increases the risk of insulin resistance and helps explain the rising incidence of the disease (Dludla et al., 2023). Type 2 diabetes mellitus (T2DM) accounts for around 90% of cases (Ahmad et al., 2022). Despite improvements in awareness (36.5%), treatment (32.2%) and control (49.2%), these indicators remain insufficient. Notably, regional disparities persist, with the fastest growth in diabetes prevalence occurring in low- and middle-income countries, thereby exacerbating global health inequalities.

The pathogenesis of diabetes mellitus is multifactorial and remains incompletely elucidated. The main mechanisms underlying the development of type 2 diabetes mellitus (T2DM) include impaired insulin secretion by pancreatic β-cells and reduced tissue sensitivity to insulin. These processes are accompanied by chronic low-grade inflammation, oxidative stress and dyslipidaemia (Młynarska et al., 2025). While current pharmacotherapeutic strategies, such as oral hypoglycaemic agents and insulin therapy, are effective, they are frequently linked to adverse effects, including hypoglycaemia, hepatic and renal impairment, and do not entirely prevent the progression of complications (Gieroba et al., 2025). Consequently, there is a growing interest in complementary and integrative therapeutic approaches aimed at improving long-term outcomes and minimising side effects.

In this context, phytotherapy is receiving increasing attention. According to estimates by the World Health Organization (WHO), around 4 billion people in developing countries use medicinal plants to treat metabolic disorders (Ekor, 2013). Experimental and clinical studies provide evidence of the antihyperglycaemic, hypolipidaemic, antioxidant and insulin-mimetic properties of natural compounds (Rahman et al., 2022). Bioactive plant constituents, including flavonoids, saponins, phenolic compounds, terpenoids and steroids, exert pleiotropic effects by modulating carbohydrate and lipid metabolism (Al-Ishaq et al., 2019; Mahapatra et al., 2025; Mohammed et al., 2025). Importantly, these multi-target mechanisms may offer advantages over single-target synthetic drugs in complex metabolic diseases such as type 2 diabetes mellitus.

Phytotherapy has a long tradition in the management of diabetes; however, it is only in recent decades that systematic scientific data have emerged to support its efficacy. The most extensively studied plants include cinnamon (*Cinnamomum* spp.), sesame (*Sesamum indicum*), aloe vera (*Aloe vera*), ginger (*Zingiber officinale*), garlic (*Allium sativum*) and turmeric (*Curcuma longa*). The active compounds in these plants have been shown to reduce blood glucose and glycated hemoglobin (HbA1c) levels, improve insulin sensitivity and have antioxidant properties. This makes them a promising addition to therapeutic strategies (Huang et al., 2023; Paudel et al., 2025; Saini et al., 2025; Tian et al., 2025). Additionally, some of these plant-derived compounds may influence the composition of the gut microbiota, which is increasingly recognised as an important factor in metabolic regulation.

This study aims to summarise the current literature on the effectiveness of commonly used medicinal plants and plant-derived products in the treatment of type 2 diabetes mellitus. It analyse their bioactive components and mechanisms of action and evaluate the potential benefits and risks of using them in clinical practice. The study also aims to identify gaps in existing research and highlight areas for future study to support the evidence-based integration of phytotherapy into diabetes care.

Material and Methodology

Study design

This study is based on a narrative literature review of peer-reviewed scientific publications that focus on the potential of medicinal plants and dietary bioactive compounds for treating diabetes. A comprehensive analysis of *in vitro*, *in vivo*, and clinical studies was performed.

Data sources and search strategy

Scientific data were retrieved from major academic databases, including PubMed, Scopus, Web of Science, and Google Scholar. The search was conducted using keywords such as "type 2 diabetes mellitus", "medicinal plants", "phytotherapy", "polyphenols", "flavonoids", "insulin resistance", "glucose metabolism", as well as the names of individual plant species.

Eligibility criteria

Studies were selected based on their relevance to glucose metabolism, insulin signalling, oxidative stress, lipid metabolism, and clinical outcomes in diabetic or prediabetic models. Only peer-reviewed English-language original articles, experimental studies, clinical trials, and systematic reviews were included.

Data extraction and synthesis

The extracted data were qualitatively analysed and organised according to plant species, identified bioactive compounds, and reported mechanisms of antidiabetic action.

Statistical analysis

The data were qualitatively analysed and grouped according to plant species, bioactive compounds, and mechanisms of antidiabetic action. No statistical meta-analysis was performed due to heterogeneity in study designs.

Results and Discussion

Up to 58.5% of patients with diabetes use phytotherapy (Kifle et al., 2021). Herbal remedies can be used either as a single plant or as part of a complex formulation. GlycaCare-II, for example, is a supplement containing cinnamon, bitter melon, Vijaysar, *Gymnema sylvestre*, *Syzygium cumini* extract and the bioavailability enhancer piperine. Majeed et al. (2021) demonstrated that this formulation is as effective as metformin at reducing glycated haemoglobin (HbA1c) and fasting blood glucose (FBS) levels. Similar herbal preparations, such as Diabecon, Diasulin and pancreatic tonics, are also widely available on the market. These products are often used as complementary therapies alongside conventional pharmacological treatment, particularly in regions with strong herbal medicine traditions. However, one of the key challenges associated with such formulations is the uncertainty surrounding their active ingredients, which makes it difficult to evaluate their therapeutic efficacy and standardise them. To ensure the reliability of results and the safety of use, it is necessary to identify the principal bioactive components and establish their dose-dependent effects. Standardisation, quality control and well-designed clinical trials are critical for integrating phytotherapeutic agents into evidence-based medicine.

The most commonly included plant components are cinnamon, cumin, sesame, aloe vera, ginger, garlic and turmeric. These have all been used in traditional medicine for centuries. Their dosages, efficacy and active compounds are summarised in Table 1. Notably, many of these plants have pleiotropic effects, including

Table 1 Most commonly used plant products in the treatment of diabetes mellitus

Plant products	Active compounds	Plant parts	Dose	Reduction in FBS ($mg \cdot dL^{-1}$)	Reduction in HbA1c (%)	References
Cinnamon	type A procyanidin polymer	bark	0.5–6.0 g	2–111	0–1.2	Sharma et al., 2012; Hasanzade et al., 2013
Cumin	thymoquinone	seeds	0.1–0.5 g	3–56	1.0–1.8	Jafari et al., 2016; Hendre et al., 2020
Sesame	sesamin	seeds	0.2 g or 30.0 mL	34–52	0.7–1.1	Mohammad Shahi et al., 2017; Aslam et al., 2019
Aloe	acemannan	leaf	600–1,000 g	13–44	0.4–0.7	Maurya et al., 2017
Ginger	gingerol, shogaol	rhizome	1.6–2.0 g	10–29	0.04–1.1	Carvalho et al., 2020
Garlic	allicin	bulb	0.9–1.5 g	4–10	0.2–0.8	Kumar et al., 2013
Turmeric	Curcumin	rhizome	0.5–2.1 g	2–9	0.02–0.9	Adab et al., 2019

the modulation of glucose metabolism, antioxidant activity and anti-inflammatory properties. These effects may collectively contribute to improved metabolic control.

While these data suggest promising glucose-lowering effects, the variability in study design, dosage and extract composition means they must be interpreted with caution and validated in large-scale randomised controlled trials.

Natural products with antihyperglycemic effects are discussed below.

Cinnamon (*Cinnamomum verum* J. Presl., *Cinnamomum cassia* (L.) J. Presl.)

Cinnamon bark has traditionally been used as both a spice and a medicinal agent, including in the management of diabetes mellitus. It is obtained from the inner bark of the shoots of *C. verum* or *C. cassia*, both of which belong to the Lauraceae family (Figure 1).

The main active constituents are cinnamaldehyde, eugenol and coumarin, the concentrations of which differ significantly between species: *C. verum* contains 50–63% cinnamaldehyde and only trace amounts of coumarins, whereas *C. cassia* contains up to 95% cinnamaldehyde and higher levels of coumarins (Ranasinghe et al., 2013). Long-term intake of coumarins is associated with an increased risk of hepatotoxicity, so *C. verum* is considered safer for long-term use (Sproll et al., 2008; EFSA, 2008). This distinction is clinically important when considering cinnamon supplementation in long-term metabolic interventions, particularly in patients with comorbid liver conditions.

Systematic reviews suggest that adding cinnamon to food or using it alongside standard hypoglycaemic agents may reduce fasting blood glucose, HbA1c, triglycerides and LDL cholesterol, while increasing HDL cholesterol (Allen et al., 2013; Costello et al., 2016). However, randomised controlled trials (RCTs) have produced conflicting results. For example, Sharma et al. (2012) demonstrated that taking 3–6 g of cinnamon powder for three months significantly reduced HbA1c and fasting blood sugar (FBS) levels in patients newly diagnosed with diabetes. However, other studies have reported no significant effect (Hasanzade et al., 2013; Talaei et al., 2017).

These discrepancies may be explained by differences in study duration, dosage, plant composition and patient characteristics. For instance, an RCT by Zare et al. (2019) found that the effects of cinnamon were significantly more pronounced in patients with a higher BMI (BMI ≥27), where glycemic improvement was accompanied by enhanced insulin resistance, as measured by HOMA-IR. This suggests that cinnamon may be particularly effective in overweight individuals, potentially improving insulin resistance by modulating gut microbiota and stimulating insulin-related pathways (Mirmiranpour et al., 2020). Such findings suggest that patient stratification is crucial for identifying those who will respond to cinnamon-based interventions.

Cinnamaldehyde has been shown to promote insulin release, enhance insulin sensitivity, stimulate hepatic glycogen synthesis, inhibit glucosidase activity, activate glucose transporter-4 (GLUT-4) and upregulate peroxisome proliferator-activated receptor (PPAR) expression (Qin et al., 2004; Kim et al., 2006; Subash

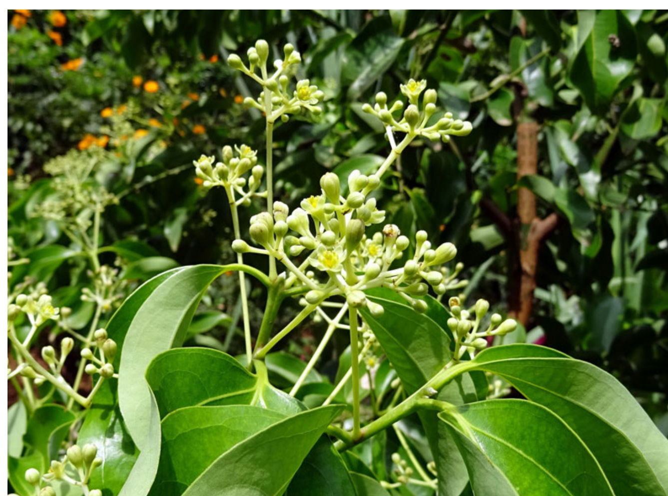

Figure 1 Cinnamon (*Cinnamomum verum* J. Presl., *Cinnamomum cassia* (L.) J. Presl.).
Source: https://saluvet.de/en/dictionary/cinnamon-cinnamomum-verum-cassia

Table 2 Main active components of *Cinnamomum* spp. and its effects on glycemic control and safety in T2DM

Species	Active components	Hypoglycemic and antidiabetic effects	Characteristics and safety	References
***Cinnamomum verum* J. Presl**	cinnamaldehyde (50–63%), eugenol, trace coumarins	insulin secretion stimulation, improved insulin sensitivity, regulation of PTP1B and insulin receptors, improved glycemic control, inhibition of pancreatic and intestinal amylase and glucosidase, increased PPAR expression	lower coumarin content → potentially safer for long-term use	Archer, 1988; Subash Babu et al., 2007; Anand et al., 2010; Ulbricht et al., 2011; Ranasinghe et al., 2013
***Cinnamomum cassia* (L.) J. Presl**	cinnamaldehyde (up to 95%), coumarins (up to 1%), benzaldehyde, methoxycinnamaldehyde	similar effects on blood glucose and insulin, stimulation of insulin receptors and PTP1B, improved insulin sensitivity	higher coumarin content → risk of hepatotoxicity with long-term use; EFSA recommends ≤0.1 $mg \cdot kg^{-1}$ body $weight \cdot day^{-1}$	EFSA, 2008; Sproll et al., 2008; Abraham et al., 2010; Ranasinghe et al., 2013
General effects of *Cinnamomum*	cinnamaldehyde, eugenol, coumarins, other phytochemicals	moderate reduction in fasting glucose and HbA1c, decreased triglycerides, total cholesterol and LDL, increased HDL, improved insulin sensitivity and glucose metabolism	activity depends on species and composition; clinical efficacy requires further high-quality studies	Akilen et al., 2012; Bandara et al., 2012; Leach and Kumar, 2012; Ranasinghe et al., 2012; Allen et al., 2013; Costello et al., 2016

Babu et al., 2007; Anand et al., 2010). Due to these properties, cinnamon is considered a promising nutraceutical for glycemic control in type 2 diabetes mellitus.

Table 2 summarises the key bioactive components of various cinnamon species, focusing on *C. verum* and *C. cassia*, and their hypoglycaemic and anti-diabetic effects. It also highlights differences in the safety profiles of different species, particularly regarding coumarin content and its implications for long-term use.

While cinnamon shows promise in terms of its metabolic effects, variability in its composition, dosage and study design highlights the need for standardised extracts and large-scale, well-controlled clinical trials to confirm its therapeutic potential in T2DM.

Sesame (*Sesamum indicum* L.)

Sesame (Figure 2) is an annual plant belonging to the Pedaliaceae family. It has traditionally been used in nutrition and folk medicine due to its rich composition of biologically active compounds, which may influence metabolism and the body's antioxidant status (Wei et al., 2022). Sesame seeds are widely used in cooking and as a potential way to help control blood glucose in people with type 2 diabetes (Aslam et al., 2017; Ghoreishi et al., 2022). Recently, sesame has also gained attention as a functional food ingredient with potential applications in the management of metabolic diseases.

The active components of sesame include polyunsaturated and monounsaturated fatty acids (PUFAs and MUFAs), as well as lignans such as sesamin, sesamolin and sesaminol. These compounds exhibit antioxidant and anti-inflammatory properties (Pathak et al., 2014; Ouboulbiga et al., 2023; Jafari et al., 2025). They may reduce levels of the pro-inflammatory cytokine TNF-α, protect pancreatic β-cells, improve insulin secretion and sensitivity, and regulate glucose and lipid metabolism (Yargholi et al., 2021; Hadipour et al., 2023; Parsa et al., 2024; Atefi et al., 2025). Such multi-target actions are particularly relevant in the context of complex metabolic disorders such as T2DM, where inflammation and oxidative stress play central roles.

Experimental and clinical studies suggest that consuming sesame seeds may lower fasting blood glucose (FBS) and HbA1c levels, though no consistent effect on fasting insulin levels has been observed (Mohammad Shahi et al., 2017; Ghoreishi et al., 2022). Furthermore, research suggests that sesame may reduce body fat percentage and improve anthropometric parameters, thereby contributing to glycemic regulation (Raeisi-Dehkordi et al., 2018).

Sesame lignans, particularly sesamin, have been shown to stimulate glycogen synthesis, enhance cellular glucose uptake, improve insulin signalling pathways and increase adiponectin levels. These effects are

Figure 2 Sesame (*Sesamum indicum* L.).
Source: https://www.ayurera.it/sesamum-indicum/

associated with better glycaemic control (Sankar et al., 2011; Mohammad Shahi et al., 2017; Aslam et al., 2019; Huang et al., 2023). Furthermore, modulation of adipokine secretion could be an important mechanism through which sesame intake improves insulin sensitivity.

While sesame is generally considered safe for adults without an allergic predisposition when consumed in moderate amounts, excessive intake may cause gastrointestinal irritation. There have been reports of allergic and anaphylactic reactions, highlighting the need for further studies to evaluate the long-term safety and efficacy of sesame in patients with T2DM (Adatia et al., 2017; Gangur and Acharya, 2021). Therefore, individual tolerance and potential allergenicity must be considered when recommending sesame-based interventions.

Table 3 presents the major bioactive components of sesame seeds and their associated biological effects, particularly with regard to glucose regulation and metabolic health. It emphasises the underlying mechanisms that contribute to improved glycemic control and insulin sensitivity, including antioxidant activity, modulation of insulin signalling and reduction of inflammation.

Thus, sesame exhibits multi-component pharmacological activity and may be considered a promising adjunct for glycemic control and improvement of metabolic status in patients with type 2 diabetes mellitus. However, additional clinical studies are required to establish definitive recommendations. Future research should focus on standardised extracts, optimal dosing strategies and long-term clinical outcomes.

Table 3 Biological properties and active components of sesame seeds

Components	Main effects	Mechanisms of action	References
Lignans (sesamin, sesamolin, sesaminol)	antioxidant activity, glucose regulation	increased glycogen synthesis, enhanced cellular glucose uptake, stimulation of insulin signaling	Pathak et al., 2014; Oboulbiga et al., 2023; Jafari et al., 2025
Monounsaturated and polyunsaturated fatty acids (MUFA, PUFA)	improved insulin sensitivity and glycemic control	increased GLP-1 secretion, modulation of lipid metabolism gene expression, and reduced insulin resistance	Yargholi et al., 2021; Hadipour et al., 2023; Parsa et al., 2024; Atefi et al., 2025
Adiponectin	increased circulating hormone levels	improved glycemic control	Mantzoros et al., 2005
Antioxidants (general)	protection of pancreatic β-cells	reduction of TNF-α, decreased inflammation, and improved insulin secretion	Wu et al., 2019; Atefi et al., 2025
Effects on anthropometric parameters	reduction of fat mass, improved metabolism	decreased production of inflammatory adipocytokines	Raeisi-Dehkordi et al., 2018

Aloe vera (*Aloe vera* L.)

Aloe vera is a perennial succulent plant belonging to the Asphodelaceae family (Figure 3). It has long been used in traditional medicine to treat skin disorders, wounds and inflammatory conditions, as well as metabolic diseases such as diabetes mellitus (Surjushe et al., 2008; Foster et al., 2011). Preparations derived from *Aloe vera* leaves, such as juice, gel and extracts, contain anthraquinones, saponins, polysaccharides, phenolic acids, vitamins and minerals. These contribute to a broad spectrum of pharmacological activities (Matei et al., 2025; Mensah et al., 2025). Due to its complex composition, *Aloe vera* is increasingly recognised as a multifunctional therapeutic agent with potential applications in the treatment of metabolic and inflammatory disorders.

The active compounds found in aloe vera include aloin, aloe-emodin, salicylates and acemannan, a bioactive polysaccharide which exhibits immunomodulatory, anti-inflammatory and anti-hyperglycaemic properties (Bai et al., 2023). Studies have shown that aloe vera can reduce hyperglycaemia, hyperlipidaemia and oxidative stress in streptozotocin-induced diabetic models, as well as protect pancreatic beta cells from damage (Suksomboon et al., 2016; Deora and Venkatraman, 2022; Haghani et al., 2022). The protection of β-cells is particularly important as preserving endogenous insulin secretion is key to slowing diabetes progression.

Clinical trials indicate that consuming *Aloe vera* preparations can significantly reduce fasting blood glucose (FBS) and HbA1c levels, improve HOMA-IR and insulin indices, and have beneficial effects on body weight and lipid profiles in patients with prediabetes and type 2 diabetes mellitus (Devaraj et al., 2013; Zhang et al., 2016). Meta-analyses suggest that the most pronounced effects are observed with treatment durations of more than 8 weeks and doses of around 200 mg per day, especially when taken in capsule or juice form (Suksomboon et al., 2016; Zhang et al., 2016). However, some randomised controlled trials have reported no significant effect on HbA1c, potentially due to differences in dosage, treatment duration and patient characteristics (Bunyapraphatsara et al., 1995). This variability highlights the importance of standardised formulations and well-designed clinical protocols in future research.

A. vera is generally considered safe when consumed in moderate amounts. However, excessive intake may lead to adverse effects, such as gastrointestinal irritation. There have also been reports of allergic reactions, highlighting the need for further long-term studies to fully assess its safety and efficacy (Guo and Mei, 2016). Additionally, potential interactions with conventional antidiabetic medications must be considered when using *A. vera* as an adjunct therapy.

Table 4 summarises the key bioactive components of *A. vera* and their biological properties, focusing on their anti-hyperglycaemic, antioxidant and anti-inflammatory effects. It also outlines the main mechanisms of action, which include the protection

Figure 3 *Aloe vera* (*Aloe vera* L.)
Source: https://planetdesert.com/

Table 4 Biological properties and active components of *Aloe vera* L

Components	Main effects	Mechanisms of action	References
Acemannan (polysaccharide)	antihyperglycemic, immunomodulatory	protection of pancreatic β-cells, stimulation of insulin secretion, and reduction of inflammation	Sánchez et al., 2020; Bai et al., 2023
Anthraquinones (aloin, aloe-emodin)	antioxidant, anti-inflammatory	reduction of oxidative stress, modulation of pro-inflammatory cytokines	Cordiano et al., 2025
Saponins	hypolipidemic, antibacterial	reduction of cholesterol and triglyceride levels, modulation of gut microbiota	Foster et al., 2011; Cao et al., 2024
Phenolic acids and salicylates	antioxidant, anti-inflammatory	inhibition of free radical processes, reduction of tissue damage	Catalano et al., 2024
Vitamins (C, E, β-carotene) and minerals	antioxidant protection, metabolic support	maintenance of homeostasis, reduction of oxidative stress	Devaraj et al., 2013; Sánchez et al., 2020

of pancreatic β-cells, the modulation of inflammation and the reduction of oxidative stress. These mechanisms contribute to improved metabolic homeostasis.

Thus, *A. vera* exhibits multi-component pharmacological activity and is therefore a promising adjunct in the management of type 2 diabetes mellitus and metabolic syndrome, particularly in obese patients with dyslipidaemia. Its combined antihyperglycaemic, antioxidant and anti-inflammatory effects make it a valuable candidate for integrative therapeutic strategies.

Ginger (*Zingiber officinale* Roscoe)

Ginger is a perennial plant belonging to the Zingiberaceae family (Figure 4). Traditionally used in Chinese and Ayurvedic medicine, it is also a popular culinary spice thanks to its distinctive flavour and aroma (Grzanna et al., 2005; Zhu et al., 2018). Its rhizomes and extracts are widely used to manage arthritis, rheumatism, asthma, gastrointestinal disorders, non-alcoholic fatty liver disease, nausea and diabetes mellitus (Mohammadzadeh Honarvar et al., 2019; Gumbarewicz et al., 2022). In recent years, ginger has attracted growing scientific interest as a functional food with potential metabolic and anti-inflammatory benefits.

The bioactive compounds found in ginger can be categorised as either volatile components, such as the terpenes zingiberene, β-bisabolene and citral, which are responsible for the aroma, or non-volatile phenolic compounds. The most extensively studied compound is 6-gingerol, which gives ginger its pungent taste. Its derivatives, shogaols and zingerone, are formed during thermal processing or storage (Cisowski et al., 2004; Arcusa et al., 2022). 6-gingerol and 6-shogaol are considered the primary antihyperglycaemic agents (Wang et al., 2013; Misawa et al., 2015). These

Figure 4 Ginger (*Zingiber officinale* Roscoe)
Source: https://www.seedsforgarden.com/

compounds are also known to exert synergistic effects, enhancing their overall biological activity.

Experimental studies indicate that ginger extracts can reduce insulin resistance, modulate peroxisome proliferator-activated receptor (PPAR) activity, decrease adipocyte size, activate thermogenesis in adipose tissue and improve gut microbiota that has been altered by a high-fat diet (Misawa et al., 2015; Wang et al., 2017, 2020). These effects are particularly relevant given the strong association between obesity and the development of type 2 diabetes mellitus (Kleinert et al., 2018). Ginger's ability to influence metabolic and inflammatory pathways makes it a promising candidate for integrative metabolic therapies.

Although somewhat heterogeneous, clinical studies have generally reported positive outcomes. Consuming 1.2–3.0 g of ginger powder over a period of 2–3 months has been shown to reduce fasting blood glucose (FBS) by 19–29 mg·dL^{-1} and HbA1c by 0.4–0.7% (Shidfar et al., 2015; Makhdoomi et al., 2017; Carvalho et al., 2020). However, some randomised controlled trials did not confirm a significant effect on HbA1c, although they did report reductions in insulin resistance (Mahluji et al., 2013). Meta-analyses conclude that ginger significantly reduces FBS and HbA1c, improves pancreatic function, and lowers the risk of metabolic syndrome (Zhu et al., 2018). However, variability in study design, dosage and patient populations highlights the need for further standardised clinical trials.

Table 5 summarises the main bioactive compounds found in ginger and their respective antidiabetic, antioxidant and anti-inflammatory properties. It also outlines the key mechanisms of action, which include modulating insulin sensitivity, reducing oxidative stress and inflammation, and improving glucose and lipid metabolism.

Ginger exhibits multi-component pharmacological activity and may therefore be considered a promising adjunct in the management of type 2 diabetes mellitus and metabolic syndrome, particularly in obese patients with dyslipidaemia. Its combined antihyperglycaemic, antioxidant and anti-inflammatory effects support its potential role in comprehensive metabolic control strategies.

Garlic (*Allium sativum* L.)

Garlic (Figure 5) is a perennial plant belonging to the Amaryllidaceae family and has long been used in traditional medicines across various cultures, including Egyptian, Chinese and Indian systems. It is also used as a culinary spice thanks to its distinctive flavour and aroma (Ayaz and Alpsoy, 2007). Garlic bulbs and extracts are widely used to manage infectious diseases, atherosclerosis, hypertension, dyslipidaemia, metabolic syndrome and diabetes mellitus, and for their immunomodulatory and anticancer properties (El-Saber Batiha et al., 2020; Tesfaye, 2021). Modern research increasingly recognises garlic as a functional food with potential cardiometabolic benefits, particularly in chronic non-communicable diseases.

Table 5 Bioactive components of ginger (*Zingiber officinale* Roscoe), their effects, and mechanisms of action

Components	Main effects	Mechanisms of action	References
6-Gingerol	antihyperglycemic, antioxidant, anti-inflammatory	increased insulin sensitivity, regulation of PPAR, reduction of adipocyte size, activation of thermogenesis in adipose tissue	Wang et al., 2013; Misawa et al., 2015; Arcusa et al., 2022
6-Shogaol	antihyperglycemic, anti-inflammatory	reduction of insulin resistance, inhibition of pro-inflammatory cytokines, and modulation of gut microbiota	Misawa et al., 2015; Wang et al., 2020
Zingerone, gingerdiones, gingerdials	antioxidant, anti-inflammatory	reduction of oxidative stress and lipid peroxidation markers, support of pancreatic β-cells	Cisowski et al., 2004; Bhandari et al., 2005
Terpenes (zingiberene, ar-curcumene, β-bisabolene, citral, etc.)	antioxidant, cardioprotective	modulation of lipid metabolism, reduction of atherosclerosis risk, and improvement of vascular function	Wei et al., 2005; Koch et al., 2017; Jabborova et al., 2022
Powdered rhizome extracts	antidiabetic	regulation of HOMA-IR, INS, FBG, HbA1c; reduction of body weight; improvement of glucose and lipid metabolism	Kadnur and Goyal, 2005; Elshater et al., 2009; Zhu et al., 2018
Phenolic compounds (other gingerols, phenylalkane derivatives)	antioxidant, anti-inflammatory	inhibition of free radical processes, protection of β-cells, and reduction of pro-inflammatory cytokines	Misawa et al., 2015; Wang et al., 2017

Figure 5 Garlic (*Allium sativum* L.)
Source: https://www.gardenia.net/plant/allium-sativum

Garlic contains several bioactive compounds, including volatile sulphur-containing components such as allicin, diallyl disulfide and diallyl trisulfide, as well as more stable derivatives formed during processing or storage, such as S-allylcysteine and S-allylmercaptocysteine. Allicin is formed when garlic cloves are mechanically disrupted and is responsible for the characteristic odour. Stable compounds such as S-allylcysteine exhibit strong antioxidant and antidiabetic effects (Shang et al., 2019; El-Saber Batiha et al., 2020; Corona-España et al., 2025). It is important to note that the stability and bioavailability of these compounds can vary significantly depending on the preparation method used, which may affect their therapeutic efficacy.

Experimental studies demonstrate that garlic extracts reduce insulin resistance, enhance AMP-activated protein kinase (AMPK) activity, inhibit lipogenesis and decrease oxidative stress and pro-inflammatory cytokine levels (Liu et al., 2012; Miki et al., 2017; Mejía Delgado et al., 2025). Furthermore, improvements in gut microbiota composition and reductions in hepatic fat accumulation have been observed, which are particularly relevant for patients with non-alcoholic fatty liver disease and metabolic syndrome (Pourreza et al., 2022). These findings suggest that garlic may exert systemic metabolic benefits through direct biochemical pathways and modulation of the gut-liver axis.

Table 6 Bioactive components of garlic (*Allium sativum* L.), their effects, and mechanisms of action

Components	Main effects	Mechanisms of action	References
Allicin (volatile sulfur compound)	antihyperglycemic, antibacterial, cardioprotective	increased insulin sensitivity, activation of AMPK, inhibition of cholesterol synthesis, and antimicrobial activity	El-Saber Batiha et al., 2020; Subramanian et al., 2020; Savairam et al., 2023
Diallyl disulfide, diallyl trisulfide	antioxidant, hypolipidemic, anti-inflammatory	reduction of ROS, inhibition of NF-κB, and modulation of lipid metabolism	Song et al., 2021; Mitra et al., 2022
S-allylcysteine (stable derivative)	antihyperglycemic, antioxidant	protection of β-cells, stimulation of insulin secretion, reduction of apoptosis, and enhancement of antioxidant enzyme activity	Saravanan and Ponmurugan, 2010, 2013; Sathibabu Uddandrao et al., 2016
S-allylmercaptocysteine	hypolipidemic, antihypertensive	reduction of cholesterol synthesis, improvement of endothelial function, and vasodilation	Rais et al., 2023; Sleiman et al., 2024
Flavonoids and phenolic acids	antioxidant, anti-inflammatory	inhibition of free radical processes, reduction of TNF-α and IL-6 levels	Liu et al., 2012; Miki et al., 2017; Mejía Delgado et al., 2025
Vitamins (C, E) and trace elements (Se, Zn)	antioxidant protection, immunomodulatory effects	reduction of oxidative stress, support of endogenous antioxidant systems	Santhosha et al., 2013; Bayan et al., 2014

Clinical studies also support its beneficial effects. Taking 1.2–1.5 g of garlic powder or 300–600 mg of standardised garlic extract for 8–24 weeks has been shown to reduce fasting blood glucose (FBS) by 10–20 $mg \cdot dL^{-1}$ and HbA1c by 0.3–0.5%, as well as decreasing total cholesterol and triglyceride levels (Ashraf et al., 2011; Gómez-Arbeláez et al., 2013). While some randomised controlled trials have reported improvements in insulin resistance without significant changes in HbA1c, meta-analyses conclude that garlic significantly reduces glycemic parameters, blood pressure, and markers of oxidative stress (Wang et al., 2017; Zhao et al., 2024). This evidence highlights garlic's potential as a complementary intervention in comprehensive cardiometabolic risk reduction.

Table 6 summarises the main bioactive components of garlic and their anti-hyperglycaemic, antioxidant and cardioprotective effects. It also outlines the underlying mechanisms of action, including modulation of insulin sensitivity, the reduction of oxidative stress and inflammation, and the regulation of lipid metabolism.

Thus, garlic exhibits multi-component pharmacological activity and may therefore be considered a promising adjunct in the management of type 2 diabetes mellitus, metabolic syndrome, and cardiovascular complications, particularly in obese patients with dyslipidaemia and hypertension. Its combined antihyperglycaemic, hypolipidaemic, antioxidant and anti-inflammatory effects make it a valuable component of integrative therapeutic strategies.

Turmeric (*Curcuma longa* L.)

Curcuma longa L., commonly known as turmeric, has been used for thousands of years in traditional Chinese and Ayurvedic medicine as a spice and a therapeutic agent (Kocaadam and Şanlier, 2017; Figure 6). Its main bioactive compound, curcumin, exhibits immunomodulatory, antioxidant, anti-inflammatory, anticancer, anticoagulant and antiangiogenic properties (Soleimani et al., 2018; Sharifi-Rad et al., 2020). It exerts its biological activity by regulating enzymes, receptors and transcription factors, including NF-κB and TNF-α (Kotha and Luthria, 2019). These pleiotropic mechanisms make curcumin particularly relevant in the treatment of multifactorial diseases such as type 2 diabetes mellitus.

A large body of *in vitro* and *in vivo* research has demonstrated that curcumin can reduce blood glucose levels and HbA1c, as well as improve insulin sensitivity, in animals with experimentally induced diabetes (Zhang et al., 2013; Karlowicz-Bodalska et al., 2017). The mechanisms by which it acts include the inhibition of glucose-6-phosphatase and phosphoenolpyruvate carboxykinase activity, the reduction of oxidative stress and the increase of glutathione levels in pancreatic β-cells (Seo et al., 2008; Balamurugan et al., 2009). Curcumin has also been shown to have a positive effect on lipid profiles, mitochondrial function and tissue protection against diabetic complications, particularly in the brain and cardiovascular system (Rastogi et al., 2008). Taken together, these findings suggest that

Figure 6 Turmeric (*Curcuma longa* L.).
Source: https://atlas.roslin.pl/plant/

curcumin may provide both glycemic control and protection against the long-term complications of diabetes.

Despite a substantial body of experimental evidence, clinical studies in humans remain limited. Most research has focused on diabetic nephropathy, microangiopathy and retinopathy (Zhang et al., 2013). One of the major barriers to the widespread clinical application of curcumin is its low bioavailability, which results from poor solubility and rapid metabolism. Advanced delivery strategies are therefore being actively developed to enhance its efficacy, including the use of nanoparticles, liposomes, phytosomes, emulsions and controlled-release formulations (Adab et al., 2019). In clinical trials, doses ranging from 450 to 2,100 mg·day^{-1} have been used; however, reductions in fasting blood glucose (FBS) have been relatively modest (2–9 mg·dL^{-1}). Co-administration with bioavailability enhancers such as piperine has been shown to significantly improve curcumin absorption and may enhance its clinical effectiveness.

Table 7 summarises the main bioactive components of turmeric, particularly curcumin and curcuminoids, and their antidiabetic, antioxidant and anti-inflammatory properties. It also outlines the key mechanisms of action, such as the modulation of insulin sensitivity, the inhibition of pro-inflammatory pathways, and the protection against oxidative stress and diabetic complications.

Thus, curcumin demonstrates considerable potential as an adjunct in the treatment of type 2 diabetes mellitus due to its diverse biological effects. However, improving its bioavailability and conducting large-scale clinical trials are essential prerequisites for confirming its real-world efficacy. Future studies should also address optimal dosing regimens, long-term safety, and interactions with standard antidiabetic therapies.

Onion (*Allium cepa* L.)

Allium cepa L., commonly known as the onion, is a perennial herbaceous plant belonging to the Amaryllidaceae family (Figure 7). Its bulbs, whether fresh or dried, are used to manage diabetes mellitus (Governa et al., 2018). Onion has traditionally been used to treat various diseases. Its main bioactive constituents are sulfur-containing compounds (L-cysteine sulfoxides) and flavonoids (such as quercetin and its glycosides), which are responsible for its antidiabetic effects (Farag et al., 2017). These effects have been observed following administration of the plant in the form of extracts, juice, lyophilised powder or essential oil (Augusti, 1973; Gupta et al., 1977; El-Demerdash et al., 2005; Azuma et al., 2007; El-Soud and Khalil, 2010). Importantly, onions are widely available and commonly consumed, which increases their potential as a dietary adjunct in diabetes management.

The hypoglycaemic activity of A. *cepa* is mainly attributed to S-methylcysteine and flavonoids, which reduce glucose and lipid levels, decrease oxidative stress and enhance the activity of antioxidant enzymes and insulin secretion. Onion extracts have been shown to normalise the activity of hepatic enzymes such as

Table 7 Bioactive components of turmeric (*Curcuma longa* L.), their effects, and mechanisms of action

Components	Main effects	Mechanisms of action	References
Curcumin	antihyperglycemic, antioxidant, anti-inflammatory, immunomodulatory	increased insulin sensitivity, reduced glycemia (FBG, HbA1c), inhibition of glucose-6-phosphatase and phosphoenolpyruvate carboxykinase, reduced β-cell apoptosis, increased glutathione levels, inhibition of NF-κB and TNF-α	Seo et al., 2008; Balamurugan et al., 2009; Zhang et al., 2013; Karlowicz-Bodalska et al., 2017
Curcuminoids	antidiabetic, hypolipidemic, antioxidant	improved lipid profile, reduced lipid peroxidation in liver, pancreas, and aorta, stimulation of antioxidant mechanisms, reduced mitochondrial dysfunction, prevention of diabetic complications	Rastogi et al., 2008; Soleimani et al., 2018; Sharifi-Rad et al., 2020
Rhizome extracts (powder, methanolic, ethanolic)	antihyperglycemic, antioxidant, anti-inflammatory	reduced glucose and HbA1c levels, improved insulin sensitivity, regulation of lipid and carbohydrate metabolism, protection of pancreatic islets	Zhang et al., 2013; Karlowicz-Bodalska et al., 2017; Soleimani et al., 2018
Synthetic and modified forms of curcumin (nanoparticles, liposomes, emulsions)	enhanced bioavailability, antihyperglycemic, antioxidant	improved absorption, sustained release, reduced oxidative stress and inflammation, potential prevention of diabetic complications	Kotha and Luthria, 2019; Sharifi-Rad et al., 2020

Figure 7 Onion (*Allium cepa* L.)
Source: https://www.maltawildplants.com/AMRY/Allium_cepa.php

hexokinase, glucose-6-phosphatase and HMG-CoA reductase, whilst also exerting hypolipidaemic effects (Akash et al., 2014). These metabolic effects suggest that onions may simultaneously influence carbohydrate and lipid homeostasis.

Oral administration of 100 g·day^{-1} of raw A. *cepa* in patients with type 1 and type 2 diabetes significantly reduced fasting blood glucose levels and induced hypoglycaemia compared to control groups and standard drugs (Taj Eldin et al., 2010). In diabetic rats, supplementation with 7% lyophilised onion powder reduced glucose and triglyceride levels, decreased the atherogenic index and increased the HDL/total cholesterol ratio while enhancing the activity of glutathione peroxidase, glutathione reductase and glutathione S-transferase (Bang et al., 2009). These findings suggest that onion-derived compounds have combined antihyperglycaemic and cardioprotective potential.

Hyperglycaemia promotes glucose oxidation and the formation of reactive oxygen species (ROS), which disrupt signalling pathways (JAK/STAT, JNK, p38 and ERK/MAPK) and contribute to insulin resistance (Ahmad et al., 2017). The hypoglycaemic and hypolipidaemic effects of A. *cepa* are closely linked to its antioxidant capacity, free radical scavenging activity and regulation of lipid metabolism (Campos et al., 2003). Quercetin inhibits α-glucosidase and, together with rutin, enhances GLUT4 translocation and glucose uptake (Kim et al., 2011; Gautam et al., 2015). L-cysteine sulfoxides and allyl propyl disulfide act as radical scavengers, supporting redox balance and increasing the activity of superoxide dismutase

Table 8 Bioactive components of *Allium cepa* L., their effects and mechanisms of action

Components	Main effects	Mechanisms of action	References
Quercetin and glycosides	antihyperglycemic, antioxidant, hypolipidemic	inhibition of α-glucosidase, increased GLUT-4 translocation, enhanced glucose uptake, improved insulin action	Kim et al., 2011; Gautam et al., 2015
L-cysteine sulfoxides (S-methylcysteine)	antihyperglycemic, antioxidant	free radical scavenging, participation in the glutathione cycle, increased activity of superoxide dismutase and catalase, stimulation of insulin secretion	Augusti et al., 1974; Kumari and Augusti, 2002
Allyl propyl disulfide	antioxidant, antidiabetic	free radical scavenging, increased antioxidant enzyme activity, and reduced oxidative stress	Kumari and Augusti, 2002
Juice, extracts, lyophilized powder	antihyperglycemic, hypolipidemic	normalization of hexokinase, glucose-6-phosphatase, and HMG-CoA reductase activity; reduction of blood glucose and lipids; increased antioxidant enzyme activity	Augusti, 1973; El-Demerdash et al., 2005; Azuma et al., 2007; Bang et al., 2009
Essential oil	antihyperglycemic, anti-inflammatory	reduction of glucose levels, inhibition of oxidative stress, and protection of β-cells	El-Soud and Khalil, 2010
Rutin	antihyperglycemic, antioxidant	increased GLUT-4 translocation, improved glucose uptake and insulin action	Gautam et al., 2015

and catalase, partly by stimulating insulin secretion (Augusti et al., 1974; Kumari and Augusti, 2002). This multifaceted mechanism highlights the onion's potential to target several key pathways involved in diabetes pathogenesis.

S-methylcysteine sulfoxide (SMCS) exhibits antioxidant and antidiabetic effects that are comparable to those of glibenclamide and insulin. It reduces levels of malondialdehyde, hydroperoxides, and conjugated dienes in tissues while maintaining body weight and blood glucose levels in alloxan-induced diabetic rats (Kumari and Augusti, 2002). Thus, SMCS represents a promising natural compound for complementing standard diabetes therapy. Further clinical studies are required to confirm its efficacy and safety in human populations.

Table 8 summarises the major bioactive components of the onion plant and their anti-hyperglycaemic, antioxidant and hypolipidaemic effects. It also outlines the primary mechanisms of action, such as enhancing glucose uptake, modulating insulin activity and reducing oxidative stress.

Thus, A. *cepa* shows promise as both a functional food and a phytotherapeutic agent with multitarget activity in diabetes management. However, standardised dosing and well-designed clinical trials are essential for its integration into evidence-based practice.

Neem (*Azadirachta indica* A. Juss.)

Azadirachta indica A. Juss. (neem; family: Meliaceae) is a tree renowned for its wide range of biologically active compounds (Figure 8). It has been used in Ayurvedic, Chinese and Unani medicine for thousands of years to treat and prevent various diseases (Alzohairy, 2016; Gupta et al., 2017; Braga et al., 2021). The combination of its long-standing traditional use and growing experimental evidence makes neem an important candidate for integrative approaches to metabolic disorders.

The different parts of the plant, such as the flowers, leaves, seeds and bark, exhibit various effects, including anticancer, anti-inflammatory, antipyretic, antimicrobial, larvicidal, antibacterial, antiviral and antidiabetic properties. To date, more than 300 structurally diverse compounds have been identified, approximately one-third of which are limonoids (e.g. nimbolide, azadirachtin and gedunin), which modulate multiple cellular signalling pathways. Dried leaves containing oxidised tetranortriterpenes such as azadirachtins are most commonly used for diabetes treatment (WHO, 2007; Alzohairy, 2016). The primary mechanism of action involves the inhibition of α-amylase and α-glucosidase, leading to a reduced in blood glucose levels (Perez-Gutierrez et al., 2012; Ponnusamy et al., 2015). Additionally, neem-derived compounds may exert pleiotropic metabolic effects by influencing oxidative stress, inflammation, and insulin signalling pathways.

Ethanolic leaf extract (400 $mg \cdot kg^{-1}$) has been shown to reduce lipid peroxidation and exhibit anti-hyperglycaemic and anti-hypercholesterolaemic activity, as well as decreasing triglyceride levels, in alloxan-induced diabetic rats (Ekaidem et al., 2007). Aqueous extracts (400–500 $mg \cdot kg^{-1}$) normalised glucose levels, serum insulin, lipid profiles, insulin signalling molecules and GLUT4 proteins in diabetic rats and rabbits, thereby enhancing glucose utilisation in skeletal muscle (Satyanarayana et al., 2015; Khosla

Figure 8 Neem (*Azadirachta indica* A. Juss.).
Source: https://www.zdrowiebezlekow.pl/; https://www.cultivatornatural.com/

et al., 2000). The hypoglycaemic effect of *A. indica* was more pronounced in diabetic animals and comparable to glibenclamide. The pre-administration of leaf extract or seed oil prevented increases in blood glucose levels compared with control animals. This indicates the potential of neem in preventing diabetes (Khosla et al., 2000). These findings highlight the therapeutic and preventive applications of neem in glycemic control.

The activity of *A. indica* extracts has been confirmed *in vitro* and *in vivo* in streptozotocin-induced diabetic rats (200–300 $mg \cdot kg^{-1}$). Observed effects include reduced non-enzymatic glycation, inhibition of advanced glycation end-product (AGE) formation, decreased oxidative stress, increased antioxidant enzyme activity, enhanced glucose-6-phosphatase activity, elevated hepatic glycogen levels and increased plasma insulin concentrations. Reduced glucokinase activity and lipid peroxidation also contribute to the prevention of tissue damage in diabetes (Gutierrez et al., 2011; Perez Gutierrez and de Jesus Martinez Ortiz, 2014). Together, these mechanisms suggest that neem targets multiple key pathological pathways of diabetes.

Table 9 summarises the key bioactive components of *A. indica* and their antidiabetic effects in different parts of the plant. It also outlines the primary mechanisms of action, which include the inhibition of carbohydrate-digesting enzymes, the enhancement of insulin signalling and the reduction of oxidative stress.

Thus, *Azadirachta indica* is a promising multi-target phytotherapeutic agent with preventive and therapeutic potential in the management of diabetes. However, further well-designed clinical trials are necessary to establish its efficacy and optimal dosage for humans, as well as its long-term safety.

Bitter melon (*Momordica charantia* L.)

Momordica charantia (bitter melon, family Cucurbitaceae) is widely distributed in tropical and subtropical regions (Figure 9). It has been used for centuries as both a vegetable and in traditional medicine to treat diabetes mellitus (Wang et al., 2017; Xu et al., 2022). It contains proteins, polysaccharides, fatty acids, essential oils, amino acids, vitamins, phenolic compounds, alkaloids, triterpenoids, saponins and other bioactive constituents, which give it antidiabetic, antihyperglycaemic, antioxidant, anti-inflammatory, antimicrobial and anticancer properties. However, some studies report potential toxic effects under certain conditions (Jia et al., 2017). Its rich phytochemical profile and long-standing dietary use make bitter melon a particularly attractive candidate for functional nutrition and phytotherapy in the treatment of metabolic diseases.

Table 9 Active components of *Azadirachta indica* A.Juss. and their antidiabetic effects

Components	Plant parts	Antidiabetic effects	Mechanisms of action	References
Azadirachtin	leaves, seeds	reduction of blood glucose	inhibition of α-amylase and α-glucosidase	Pérez-Gutiérrez et al., 2012; Ponnusamy et al., 2015
Nimbolide	leaves	antihyperglycemic, antioxidant	modulation of signaling pathways, reduction of oxidative stress	Gupta et al., 2017; Braga et al., 2021
Gedunin	leaves	reduction of glycemia and lipids	inhibition of glucose-metabolizing enzymes, increased GLUT4, and stimulation of insulin secretion	Gupta et al., 2017; Braga et al., 2021
Tetranortriterpenes	leaves	antihyperglycemic activity	inhibition of α-amylase and α-glucosidase	Alzohairy, 2016
Seed oil	seeds	reduction of glucose, prevention of hyperglycemia	improved glucose utilization, antioxidant effects	Khosla et al., 2000
Ethanolic extract	leaves	reduction of triglycerides, antihyperglycemic	decreased lipid peroxidation, increased antioxidant enzyme activity	Ekaidem et al., 2007
Aqueous extract	leaves	normalization of glucose and insulin levels	increased GLUT4, modulation of insulin signaling molecules	Khosla et al., 2000; Satyanarayana et al., 2015
Streptozotocin-induced diabetes (*in vivo*)	leaves/ seeds	antidiabetic, antioxidant	reduced AGE formation, increased antioxidant enzymes, decreased lipid peroxidation	Gutierrez et al., 2011; Perez Gutierrez and de Jesus Martinez Ortiz, 2014

The antidiabetic effects of *Momordica charantia* are associated with the inhibition of α-glucosidase and α-amylase, the activation of AMPK, JNK and Akt signalling pathways, the regulation of protein tyrosine phosphatase 1B (PTP1B) and the inhibition of advanced glycation end-product (AGE) formation. Additionally, modulation of the gut microbiota and increased production of short-chain fatty acids (SCFAs) play an important role in improving glycaemic and lipid profiles (Zhang et al., 2020). These multitarget mechanisms highlight the potential of bitter melon to influence metabolic regulation and inflammatory pathways in diabetes.

Various forms of *M. charantia* fruit extract (e.g. juice, whole fruit, lyophilised powder and capsules) have been shown to increase the number and functionality of pancreatic islet β-cells, thereby promoting their regeneration in rats with streptozotocin- or alloxan-induced diabetes (Ahmed et al., 1998; Singh and Gupta, 2007; Cortez-Navarrete et al., 2021). Methanolic and protein extracts have been shown to improve insulin secretion and exhibit insulin-mimetic activity (Ali et al., 1993; Yibchok-Anun et al., 2006). These regenerative and insulin-like properties distinguish bitter melon from many other plant-based antidiabetic agents.

In models of a high-fat diet, lyophilised juice from unripe fruit has been shown to improve oral glucose tolerance, reduce body weight and visceral fat, increase free fatty acid concentrations and alleviate obesity, without affecting fat absorption (Chen et al., 2003). Momordicosides enhance fatty acid oxidation and glucose utilisation, thereby improving insulin sensitivity and glycaemic control (Tan et al., 2008). Furthermore, *M. charantia* has been shown to promote the healing of diabetic wounds by stimulating angiogenesis and the formation of granulation tissue, without having any systemic effects on glucose levels (Singh et al., 2017; Moulik et al., 2003). These findings suggest additional therapeutic benefits beyond glycemic control, particularly in the management of diabetes-related complications.

Clinical studies confirm the hypoglycaemic and lipid-lowering effects of *M. charantia* in patients with type 2 diabetes and prediabetes. These studies have shown improvements in fasting glucose levels, lipid profiles, atherogenic index and body weight, with no serious adverse effects (Fuangchan et al., 2011; Inayat U Rahman et al., 2015; Krawinkel et al., 2018; Kim et al., 2020). However, variability in study design, dosage and preparation forms indicates the need for standardised clinical protocols.

Figure 9 Bitter melon (*Momordica charantia* L.)
Source: https://www.picturethisai.com/pl/wiki/Momordica_charantia.html
https://mystic.garden/pl/p/Gorzki-melon-Karela-Momordica-charantia-owoc-50g/579

Table 10 Bioactive components, mechanisms of action, and biological effects of *Momordica charantia* L.

Components	Main mechanisms of action	Biological effects	References
Polysaccharides, proteins, peptides, charantins	inhibition of α-glucosidase and α-amylase; activation of AMPK, JNK, Akt; regulation of PTP1B; inhibition of AGE formation	hypoglycemic effect, increased insulin sensitivity, improved glycemic control	Sur et al., 2018; Pahlavani et al., 2019
Momordicosides, triterpenoids	enhancement of fatty acid oxidation, increased glucose utilization	antihyperlipidemic effects, reduction in body weight and visceral fat	Chen et al., 2003; Tan et al., 2008
Fruit juice and extracts (methanolic, protein fractions)	stimulation of insulin secretion, regeneration of pancreatic β-cells	increased β-cell number, improved islet function, reduced glycemia	Ahmed et al., 1998; Yibchok-anun et al., 2006; Cortez-Navarrete et al., 2021
Lyophilized juice of unripe fruits	modulation of gut microbiota, ↑ SCFA production	hypoglycemic and lipid-lowering effects, reduction of obesity	Chen et al., 2003; Zhang et al., 2020
Fruit extracts (alcoholic, aqueous)	increased hepatic glucose utilization	improved oral glucose tolerance	Sarkar et al., 1996
Topical fruit extracts	stimulation of angiogenesis and tissue regeneration	improved healing of diabetic wounds	Moulik et al., 2003; Singh et al., 2017
Clinical studies (powder, juice, extracts)	reduction of fasting glucose and fructosamine levels, improvement of lipid profile	efficacy in type 2 diabetes and prediabetes without serious adverse effects	Fuangchan et al., 2011; Inayat U Rahman et al., 2015; Kim et al., 2020

Table 10 summarises the main bioactive components of *M. charantia* and their antidiabetic and metabolic effects. It emphasises the key mechanisms of action, such as the modulation of glucose metabolism, the enhancement of insulin secretion and sensitivity, and the regulation of lipid metabolism and gut microbiota.

Thus, *M. charantia* exhibits multi-target antidiabetic properties, including antihyperglycaemic, hypolipidaemic, antioxidant, anti-inflammatory and beta-cell regenerative effects. These properties make it a promising agent for treating and preventing diabetes mellitus and its complications associated with dyslipidaemia and obesity. Further large-scale, well-controlled clinical trials are necessary to determine the optimal dosage, long-term safety and compatibility with conventional therapies.

Tulsi (*Ocimum tenuiflorum* L.)

Ocimum tenuiflorum L., commonly known as tulsi or holy basil (Figure 10), is a sacred medicinal plant in India that has traditionally been used in the Ayurvedic, Siddha and Unani systems of medicine (Cohen, 2014; Mohan Gowda et al., 2023). Belonging to the Lamiaceae family, it is a herb or shrub growing up to 1 m in height and is widely distributed in India, parts of Africa, China and Taiwan. The medicinal raw material consists of the fresh or dried leaves (WHO, 2002), which are rich in tannins and essential oils containing eugenol, methyleugenol and caryophyllene (Pattanayak et al.,

Figure 10 Tulsi (*Ocimum tenuiflorum* L.). Source: https://www.gardenia.net/plant/ocimum-sanctum

2010). Tulsi is also notably classified as an adaptogenic plant, meaning it may help the body cope with metabolic stress and improve overall homeostasis. This is particularly relevant in chronic conditions such as type 2 diabetes.

Early clinical evidence (Agrawal et al., 1996) showed that giving *O. tenuiflorum* to patients with non-insulin-dependent diabetes significantly lowered their fasting and postprandial blood glucose levels and moderately reduced their total cholesterol. Subsequently, a pilot study (Satapathy et al., 2017) confirmed that supplementation with the plant extract reduced insulin resistance by ~25–28%, normalised lipid profiles and contributed to weight loss in overweight individuals. These findings suggest that tulsi may have glycemic and cardiometabolic benefits, addressing multiple components of metabolic syndrome simultaneously.

Further support for its antihyperglycaemic and antidyslipidaemic effects comes from experimental studies in animal models. Aqueous extracts (200 mg·kg^{-1}) have been shown to reduce insulin resistance, correct dyslipidaemia and increase the activity of antioxidant enzymes, thereby lowering oxidative stress (Hussain et al., 2001; Reddy et al., 2008). Ethanolic extracts (80%) enhanced the action of exogenous insulin and stimulated its secretion by pancreatic β-cells (Chattopadhyay, 1993; Hannan et al., 2006). This dual mechanism, which improves insulin sensitivity while also enhancing insulin secretion, may be particularly advantageous in the management of type 2 diabetes.

Further studies have confirmed its anti-dyslipidaemic and antioxidant properties. Leaf extract (500 mg·kg^{-1}) was found to reduce glycaemia, HbA1c levels, free fatty acids and hepatic fat accumulation by activating enzymes involved in lipid metabolism (Husain et al., 2015). Non-volatile oil, which is rich in α-linolenic acid, exhibited antioxidant and hypoglycaemic effects by stimulating insulin secretion in diabetic rats (Suanarunsawat et al., 2016). However, a tetracyclic triterpenoid isolated from the plant's aerial parts was found to reduce glucose and triglyceride levels, though it may also adversely affect cholesterol levels (Patil et al., 2011). This highlights the need for careful safety evaluation. This emphasises the importance of standardising plant extracts and identifying specific bioactive compounds to ensure efficacy and safety in clinical use.

Table 11 summarises the results of experimental and clinical studies on *O. tenuiflorum*, highlighting its antidiabetic and metabolic effects in various models. The review shows that various plant preparations improve glycemic control, insulin sensitivity, lipid profile and antioxidant status.

Table 11 Studies on *Ocimum tenuiflorum* L. and its antidiabetic and metabolic activity

Model (human/animal)	Preparation/dose	Duration	Main effects	References
Patients with type 2 diabetes	*O. tenuiflorum*/ *O. album* leaves	crossover RCT	↓ fasting and postprandial glucose; ↓ urinary glucose; moderate ↓ cholesterol	Agrawal et al., 1996
30 young obese individuals	encapsulated extract, 250 mg ×2·day^{-1}	8 weeks	↓ plasma insulin (−28.49%); ↓ HOMA-IR (−24.79%); normalized lipid profile; ↓ BMI and body weight	Satapathy et al., 2017
Rats (insulin resistance model)	aqueous extract, 200 mg·kg^{-1}, oral	study-dependent	↓ fasting glucose; ↓ glucose intolerance; ↓ cholesterol and LDL; ↑ antioxidant enzymes (SOD, CAT, GPx, GST); ↑ reduced glutathione	Hussain et al., 2001; Reddy et al., 2008
Rats (control, hyperglycemic, STZ-diabetic)	ethanolic leaf extract (80%)	single/short-term	↓ blood glucose; ↑ effect of exogenous insulin	Chattopadhyay, 1993
Ex vivo (rat pancreas), BRIN-BD11 cell line	leaf extract	cell experiments	↑ insulin secretion from β-cells	Hannan et al., 2006
Rats (alloxan-induced diabetes)	aqueous extract, 500 mg·kg^{-1}	15 days	↓ glucose, HbA1c, LDL, free fatty acids; ↓ lipid peroxidation; ↑ LCAT and hepatic lipoprotein lipase activity	Husain et al., 2015
STZ-diabetic rats	non-volatile leaf oil, 46.54 mg·kg^{-1}·day^{-1}	3 weeks	↓ plasma glucose; ↑ insulin; ↑ antioxidant activity (linked to α-linolenic acid)	Suanarunsawat et al., 2016
Alloxan-diabetic rats	isolated triterpenoid	not specified	↓ glucose, total cholesterol, TG, HDL; ↑ LDL	Patil et al., 2011

Thus, *O. tenuiflorum* demonstrates multifactorial antidiabetic potential through its combined hypoglycaemic, anti-dyslipidaemic and antioxidant effects, as evidenced by both experimental and early clinical studies. Nevertheless, large-scale, multicentre clinical trials are required to definitively establish its efficacy and safety. Furthermore, future research should focus on dose optimisation, long-term safety and potential interactions with conventional antidiabetic medications.

Ginseng (*Panax ginseng* C.A. Meyer and *Panax quinquefolius* L.)

Ginseng has been used in traditional Chinese medicine for over 5,000 years (Mancuso and Santangelo, 2017). Of the thirteen species that have been identified, the two most commonly used are *Panax ginseng* (Korean ginseng), cultivated in China and Korea, and *Panax quinquefolius* (American ginseng), and grown in the United States and Canada (Baeg and So, 2013; Figure 11). Notably, these two species differ in both geographic origin and phytochemical composition, which may influence their pharmacological effects and clinical efficacy.

Thanks to their tonic, nootropic and adaptogenic properties, ginseng preparations are used to treat asthenia, insomnia, impotence, cardiovascular disorders and metabolic diseases, including diabetes (Xiang et al., 2008; Park et al., 2012). In 2014, the European Medicines Agency officially recognised its use as a traditional herbal medicinal product for treating asthenia (EMA, 2014). These adaptogenic properties are particularly relevant in metabolic disorders, as they may contribute to improved stress resilience and metabolic homeostasis.

The main active components are ginsenosides, which exhibit anti-inflammatory, antioxidant, and anticancer properties. However, it is important to note that ginseng may interact with medications such as warfarin, oral hypoglycaemic agents and insulin, so caution is necessary (Kiefer and Pantuso, 2003). *P. quinquefolius* contains higher concentrations of protopanaxadiols than *P. ginseng* (Wang et al., 2015). Therefore, selecting the correct ginseng species and standardising the extract is crucial for ensuring consistent therapeutic outcomes and minimising potential drug-herb interactions.

Systematic reviews report inconsistent results regarding glycaemic control. In four randomised controlled trials (0.78–6.0 g·day^{-1} for up to 12 weeks), no significant effect was observed (Kim et al., 2011). However, subsequent meta-analyses have reported

Figure 11 Ginseng (*Panax ginseng* C.A. Meyer and *Panax quinquefolius* L.).
Source: https://morningchores.com/growing-ginseng/; https://www.outsidepride.com/

modest reductions in fasting and postprandial glucose levels, though no significant changes in HbA1c have been detected (Shergis et al., 2013; Shishtar et al., 2014; Gui et al., 2016). These discrepancies may be attributed to differences in study design, duration and dosage, as well as variability in the ginseng preparations used across trials.

In vivo studies support ginseng's antidiabetic activity. For example, saponins (150–300 mg·kg^{-1}) have been shown to reduce glycaemia via the activation of GLP-1 (Liu et al., 2013), while water-soluble polysaccharides (1 g·kg^{-1}·day^{-1}) have been shown to influence energy metabolism (Niu et al., 2012). Protopanaxadiol and protopanaxatriol saponins (50–150 mg·day^{-1}) have been shown to decrease hyperglycaemia, insulin

Table 12 Studies on *Panax ginseng* C.A.Mey. and *Panax quinquefolius* L. in the context of glycemic control and diabetic complications

Study model	Preparation/dose	Duration	Main effects	References
4 RCTs, patients with T2DM	*P. ginseng* extract, 0.78–6.0 g·day^{-1}	≤ 12 weeks	no significant effect on HbA1c or glycemic control	Kim et al., 2011
16 RCTs (meta-analysis)	*P. ginseng* (various doses)	4–24 weeks	slight reduction in fasting and postprandial glucose; no effect on HbA1c	Shergis et al., 2013
Meta-analyses of RCTs	*P. ginseng* and *P. quinquefolius*	4–16 weeks	moderate reduction in glycemia; no effect on HbA1c	Shishtar et al., 2014; Gui et al., 2016
Diabetic mice	*P. ginseng* saponins, 150–300 mg·kg^{-1}	8 weeks	↓ glycemia; ↑ GLP-1 secretion	Liu et al., 2013
Diabetic mice	*P. ginseng* polysaccharides, 1 g·kg^{-1}day^{-1}	8 weeks	normalization of energy metabolism; improved insulin sensitivity	Niu et al., 2012
T2DM mice	protopanaxadiol and PPD/PT saponins, 50–150 mg·day^{-1}	6 weeks	↓ hyperglycemia; ↓ insulin resistance; ↓ TNF-α, IL-6; ↑ antioxidant activity	Deng et al., 2017
Rats with diabetic nephropathy	heat-processed ginseng 100 mg·kg^{-1}	6 weeks	improved renal function; ↓ oxidative stress	Kim et al., 2008
Diabetic mice	black ginseng, 200 mg·kg^{-1}	8 weeks	stronger effect than red ginseng: ↓ glycemia; ↑ β-cell function; ↓ apoptosis	Seo et al., 2016; Kim et al., 2016
Diabetic mice	pectin lyase-modified extract, 20–100 mg·kg^{-1}	8 weeks	↓ AGE formation; improved metabolic function	Kim et al., 2017
Mice	ginsenoside-enriched adventitious root extract	4 weeks	higher efficacy than field ginseng: ↓ glycemia and inflammation	Murthy et al., 2014

resistance and inflammation (by reducing TNF-α and IL-6 levels), while enhancing antioxidant defences (Deng et al., 2017). These findings suggest that ginseng has pleiotropic effects that target both glucose metabolism and the inflammatory pathways associated with diabetes.

Innovative extraction technologies have further enhanced the bioactivity of ginseng. Heat-processed ginseng (100 mg·kg^{-1}) has been shown to improve renal function (Kim et al., 2008), whereas black ginseng (200 mg·kg^{-1}) has demonstrated greater efficacy than red ginseng in reducing glycaemia, enhancing beta-cell function and decreasing apoptosis (Kim et al., 2016; Seo et al., 2016). Pectin lyase-modified extracts (20–100 mg·kg^{-1}) have been shown to reduce AGE formation (Kim et al., 2017), while ginsenoside-enriched adventitious root extracts have demonstrated greater efficacy than those from field-grown ginseng (Murthy et al., 2014). These advancements emphasise the importance of formulation and processing methods in enhancing the therapeutic potential of ginseng.

Table 12 summarises the results of clinical and experimental studies on *P. ginseng* and *P. quinquefolius*, with a focus on their impact on glycemic control and diabetic complications. While clinical trials report modest or no significant effects on HbA1c, experimental models consistently demonstrate improvements in glucose metabolism, insulin sensitivity, inflammation and oxidative stress.

Therefore, *Panax ginseng* and *Panax quinquefolius* show considerable potential in glycemic control and the management of diabetic complications. However, clinical findings remain inconsistent, underscoring the need for further well-designed studies. Future research should focus on standardised preparations, long-term safety and large-scale clinical trials to establish clear therapeutic guidelines.

Safety of medicinal plants

Plant-derived products are often perceived as inherently safe; however, this assumption is not fully supported by evidence. Some commonly used plants, such as garlic, cinnamon, and ginger, may increase bleeding risk, while aloe vera has been reported to prolong bleeding time (Lee et al., 2004). Gastrointestinal side effects and allergic reactions are also relatively frequent (Basch et al., 2003), and caution is warranted in patients receiving anticoagulants or undergoing surgery.

Herb-drug interactions represent another important concern. Certain plants, including aloe vera and turmeric, can modulate cytochrome P450 enzymes and drug transporters, thereby altering the pharmacokinetics

of antidiabetic drugs (Djuv and Nilsen, 2012; Neerati et al., 2014). In addition, hepatotoxicity has been associated with some herbal products, such as green tea extracts and Piper methysticum (Mazzanti et al., 2015; Soares et al., 2022).

A major limitation is the lack of standardisation of herbal preparations, as their composition may vary depending on environmental and processing factors (Firenzuoli and Gori, 2005). Cases of adulteration with synthetic drugs, including glibenclamide, have also been reported (Ching et al., 2012; Pamidimarri et al., 2019). Furthermore, contamination with heavy metals exceeding safety limits has been documented in some products (Bhalla and Pannu, 2008; Mikulski et al., 2017).

Overall, these risks highlight the need for rigorous quality control, toxicological evaluation, and greater awareness among healthcare professionals and patients to ensure the safe use of medicinal plants.

Conclusions

Type 2 diabetes mellitus remains a major global health challenge, with increasing prevalence and limitations in long-term pharmacological management. In this context, medicinal plants and their bioactive compounds represent a promising complementary approach due to their multi-target mechanisms, including the improvement of glycaemic control, enhancement of insulin sensitivity, modulation of lipid metabolism, and reduction of oxidative stress and inflammation. A number of plant species, such as cinnamon, ginger, garlic, onion, turmeric, aloe vera, cumin, neem, bitter melon, tulsi, and sesame, have demonstrated antidiabetic potential in experimental and clinical studies. However, their clinical application is limited by the lack of standardised formulations, variability in phytochemical composition, potential adverse effects, and possible interactions with conventional drugs. Overall, although phytotherapy shows considerable potential in the management of type 2 diabetes, current evidence remains heterogeneous and insufficient for definitive clinical recommendations. Future research should prioritise well-designed randomised controlled trials, standardisation of herbal preparations, and comprehensive safety assessments. An interdisciplinary approach will be essential to ensure the safe, effective, and evidence-based integration of medicinal plants into diabetes care.

Conflicts of interest

The authors have no competing interests to declare.

Ethical statement

This article does not include any studies that would require an ethical statement.

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