

# Medicinal Herbs in Metabolic Regulation: Mechanistic Insights into the Dual Management of Type 2 Diabetes and Dyslipidemia

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## Abstract

Type 2 diabetes mellitus (T2DM) and dyslipidemia commonly coexist and increase cardiovascular risk through interconnected mechanisms involving insulin resistance, oxidative stress, and chronic inflammation. While conventional pharmacological therapies effectively control metabolic abnormalities, concerns related to side effects, cost, and long-term adherence have encouraged exploration of medicinal herbs as complementary multi-target interventions. This review provides a mechanism-based overview of medicinal herbs with dual antidiabetic and antilipidemic potential, integrating evidence from both preclinical and clinical studies.

Medicinal herbs regulate metabolic homeostasis through multiple pathways, including enhancement of insulin secretion, improvement of insulin sensitivity via AMPK and PI3K/Akt signaling, inhibition of carbohydrate-digesting enzymes, modulation of lipid metabolism, and reduction of oxidative and inflammatory stress. Botanicals such as *Trigonella foenum-graecum*, *Curcuma longa*, *Momordica charantia*, *Berberis aristata*, and *Allium sativum* demonstrate overlapping mechanisms that simultaneously influence glucose and lipid regulation. Antioxidant phytochemicals further support  $\beta$ -cell protection and metabolic balance.

Despite promising mechanistic evidence, clinical translation remains limited due to variability in extract standardization, dosage, and study design, with several herbs still supported mainly by preclinical data. Future research should focus on standardized formulations and well-designed clinical trials to establish evidence-based therapeutic applications for metabolic disorders.

## 1. Introduction

Type 2 diabetes mellitus (T2DM) commonly accompanied by dyslipidemia and together they significantly increase the chances of cardiovascular risk. This interrelationship is largely driven by insulin resistance which disrupts the glycemic control and lipid metabolic pathways (Wang, 2025). Standard pharmacological treatments are effective in lowering glucose and lipid levels, however their use is limited due to side effects, affordability, and poor customer adherence, which has shifted interest in complementary herbal based therapeutic approaches due to their potential to modulate several metabolic targets (Sarker, 2024; Zhou, 2022). A broad range of bioactive phytochemicals are present in medicinal herbs and spices like saponins, flavonoids, phenolic acids, and sulfur-containing compounds, which further influence insulin secretion and its signaling, carbohydrate-digesting enzymes, lipid biosynthetic pathways, and other oxidative inflammatory processes relevant to both diabetes and dyslipidemia (Kashif,

2023; Mkhize, 2025). Despite having larger number of herbal studies, the overall quality and translational relevance of resulting evidence vary substantially. In many cases, the insights are derived largely from preclinical findings and only a limited number of herbs have been evaluated through consistent human intervention trials (Vafaeipour, 2022; Du, 2024). In this context, there is a need of mechanism-based comparative review that explicitly distinguishes between clinical and preclinical studies to (a) identify herbs with verified dual antidiabetic and antilipidemic potential, (b) reveal gaps dominated by preclinical findings, and (c) guide evidence-based selection of plant candidates for future clinical trials.

### **Metabolic Interrelationship Between Type 2 Diabetes Mellitus and Dyslipidemia**

In the insulin resistant state, the suppressive effect on adipose tissue lipolysis is reduced, leading to an increased release of free fatty acids into the circulation and their subsequent uptake by the liver. This surplus of lipid supply elevated the hepatic triglyceride synthesis and stimulates very-low-density lipoprotein (VLDL) secretion and this altered combination produces the lipid disbalance observed in diabetic dyslipidemia, marked by higher levels of triglycerides, low high-density lipoprotein cholesterol (HDL-C), and increased proportion of small dense low-density lipoprotein (LDL) particles (Jahdkaran & Sistanizad, 2025).

Dyslipidemia is highly observed among individuals with higher blood sugar, the studies indicate that the lipid abnormalities are present in up to 70–90% of affected population. Findings from clinical and population-based studies reported that abnormal lipid levels often develop during the early stages of insulin resistance and may occur overt hyperglycemia. This highlights dyslipidemia as a fundamental feature of metabolic disease rather than a secondary consequence (Jahdkaran & Sistanizad, 2025).

At the pathophysiological level, disruptions in glucose and lipid metabolism are closely linked through shared pathways involving insulin signaling, chronic low-grade inflammation, and oxidative stress. Increased lipid levels induce lipotoxic effects in insulin-sensitive tissues such as skeletal muscle, liver, and pancreatic  $\beta$ -cells, impairing glucose uptake and insulin secretion, inducing chronic hyperglycemia which in turn further disrupts lipid metabolism, reinforcing a pathological feedback loop that drives vascular damage and elevated cardiometabolic risk (Bardini et al., 2012). Some reviews recognize this cycle of interaction as a key driver of disease progression in metabolic dysfunctions (Saadati et al., 2025). Beyond insulin resistance, chronic hyperglycemia induces oxidative stress through excessive production of reactive oxygen species and impaired antioxidant defense systems. Oxidative stress damages pancreatic  $\beta$ -cells, which are particularly vulnerable due to their low endogenous antioxidant capacity, thereby worsening glycemic control. Simultaneously, oxidative modification of LDL particles accelerates atherogenesis and aggravates lipid abnormalities. Inflammatory mediators such as tumor necrosis factor- $\alpha$ , interleukin-6, and C-reactive protein further exacerbate both insulin resistance and dyslipidemia, establishing a self-perpetuating cycle linking the two disorders (Ritchie & Connell, 2007; Yaribeygi et al., 2019).

Therefore, evaluating herbs through a mechanism-oriented lens, rather than isolated outcomes, is particularly relevant for metabolic disorders that coexist and interact at multiple biochemical levels (Williamson, 2017; Salehi et al., 2019).

### **Section 2: Oxidative Stress and Inflammation — Converging Pathways in Metabolic Disease**

Many serious cardiometabolic disorders like diabetes mellitus, dyslipidaemia, etc. are known to develop due to oxidative stress and chronic low-grade inflammation. Prolonged hyperglycemia and increased free fatty acids in diabetes mellitus enhances production of reactive oxygen species (R.O.S). Overwhelming

intrinsic antioxidant defenses and creating, oxidative stress, an imbalance that short-circuits insulin signaling and damages  $\beta$ -cell integrity. Concurrently, ROS activate pro-inflammatory signalling cascades including NF- $\kappa$ B; this may promote production of cytokines, such as IL-6, and TNF- $\alpha$ . The inflammatory mediators induce inflammatory response contributing towards systemic inflammation and increased insulin resistance (Dawi et al., 2024). The relationship between the build-up of reactive oxygen species and inflammatory medications exacerbates glucose and lipid metabolism and insulin action defect.

The relationship among oxidative stress, inflammation, and metabolic syndrome is also shown by studies using a composite index, such as the oxidative balance score (OBS), which combines dietary and lifestyle behaviours associated with redox homeostasis.

Recent studies conducted on a population level indicate that higher OBS values, which reflect higher antioxidant exposure and lower exposure to oxidative stress, associate with lower risk of metabolic syndrome and its individual components: namely, dyslipidaemia, hypertension, and impaired glucose regulation. Additionally, the serious lower all-cause and cardiovascular mortality rates of the higher OBS subjects. These data suggest the clinical significance of systemic oxidative balance in metabolic regulation (Li et al., 2024; Xu et al., 2024).

The inflammatory processes are significantly linked with metabolic dysfunction by activating the innate immune signalling and recruiting immune cells infiltration to metabolically active tissues. Clinical studies suggest that inflammatory markers, such as high-sensitivity C-reactive protein (hsCRP) and interleukin- $1\beta$  (IL- $1\beta$ ), have been documented in T2DM patients with advanced atherosclerotic disease. The presence of these makers are correlated with altered lipid profiles and oxidative stress markers. The study found that lipotoxicity, oxidative stress and inflammation interact with one another to worsen the vascular damage associated with diabetes. (Ménégaud et al; 2023)

Mechanistically, oxidative stress disrupts the IRS-mediated signaling pathway of insulin while also impairing glucose transport downstream, notably PI3K/Akt. At the same time, reactive oxygen species and inflammatory cytokines develop and aggravate endothelial dysfunction by reducing nitric oxide bioavailability and increasing the expression of adhesion molecules and other inflammatory processes involved in the vessels which directly augment the metabolic and cardiovascular burden in T2DM and dyslipidemia. Hence, targeting these pathways; whether with lifestyle interventions or antioxidant therapies or through inhibition of inflammatory signaling, may reduce disease progression and complications. (Dawi et al., 2024; Li et al., 2024).

### Section 3 — Mechanistic Targets of Medicinal Herbs: Insulin Secretion & Sensitivity

#### 3.1 Herbs Modulating Insulin Secretion

Many medicinal herbs have been reported to improve glucose homeostasis through modulation of pancreatic  $\beta$ -cell activity and enhancement of insulin secretion. Among these, bitter melon (*Momordica charantia*) possesses diverse bioactive compounds that influence several metabolic pathways including inhibition of carbohydrate-digesting enzymes and stimulation of pancreatic insulin release. Its antidiabetic effects are well documented in experimental models, with limited but supportive human studies demonstrating improvements in glycemic control and lipid parameters following supplementation (Panwar, S. S. 2025).

Black seed (*Nigella sativa*) represents another extensively investigated medicinal plant, largely attributed to its principle bioactive compound, thymoquinone. Clinical trials have reported reductions in fasting blood glucose and HbA1c levels alongside improvements in pancreatic  $\beta$ -cell function and insulin

secretion. Observed decreases in inflammatory biomarkers further suggest that its insulinotropic effects may be partly mediated through anti-inflammatory mechanisms (Makhmari, et al; 2025)

Similarly, fenugreek (*Trigonella foenum-graecum*) has demonstrated both insulin-secretory and insulin-sensitizing properties. Evidence from clinical studies indicates significant glucose-lowering effects in individuals with type 2 diabetes, supporting its role in enhancing pancreatic insulin output and overall glycemic regulation (Panwar, S. S. 2025).

Other botanicals including *Punica granatum* (pomegranate) have shown the ability to stimulate pancreatic insulin gene expression and improve  $\beta$ -cell function, however, current evidence is derived predominantly from preclinical investigations, highlighting the need for well designed human trials (Chahrour et al; 2025). Mechanistic reviews consistently indicate that phytochemicals such as polyphenols, flavonoids, and terpenoids contribute to these effects by promoting  $\beta$ -cell survival, enhancing insulin gene expression, and activating signaling pathways like PI3K/Akt that support insulin secretion. These mechanisms frequently overlap with antioxidant and anti-inflammatory actions, thereby reducing glucotoxic stress and preserving  $\beta$ -cell integrity (Nazarian et al; 2018).

### 3.2 Herbs Improving Insulin Sensitivity

Improvement of insulin sensitivity is a central therapeutic target for restoring efficient glucose uptake in peripheral tissues. Many medicinal herbs influence major molecular pathways involved in insulin signaling, including AMP-activated protein kinase (AMPK), glucose transporter type-4 (GLUT4) translocation, the receptors activated by peroxisome proliferator (PPARs), and downstream components of the insulin receptor cascade.

Curcumin, the principle bioactive compound of *Curcuma longa*, has been widely investigated for its potential to regulate metabolism. Experimental and clinical evidence indicates that curcumin enhances insulin sensitivity mainly through activation of AMPK and modulation of PPAR $\gamma$  signaling. In addition to these metabolic benefits, its anti-inflammatory activity may indirectly improve insulin responsiveness by lowering cytokine-mediated interference with insulin signaling pathways (Salleh et al; 2021).

Cinnamon (*Cinnamomum zeylanicum/Cassia*) species have also attracted attention due to their potential insulin-mimetic properties. Suggested mechanisms include improved insulin receptor phosphorylation and enhanced GLUT-4 translocation in skeletal muscle and adipose tissues. Despite a number of clinical studies report slight improvements in glycemic indices, considerable heterogeneity among trials suggests that factors such as dosage, extract composition, and study duration affect outcomes (Ansari et al; 2023). Other common herbs such as ginger (*Zingiber officinale*), garlic (*Allium sativum*), and ginseng (*Panax ginseng*) appear to modulate insulin sensitivity through multiple mechanism involving glucose uptake and intracellular signaling pathways. However, on comparison with preclinical findings, human trials remain inconsistent highlighting the need for well-designed randomized trials to confirm their therapeutic relevance (Nazarian et al; 2018).

Reduction of oxidative stress represents an additional mechanism that herbal bioactives and better insulin function are interrelated. Antioxidant phytochemicals, particularly flavonoids and phenolic compounds, may suppress inflammatory signaling pathways known to impair insulin responsiveness. Therefore, herbs possessing both antioxidant capacity and primary metabolic regulatory effects may offer synergistic benefits in the management of insulin resistance (Ansari et al; 2023).

## Section 4: Mechanistic Targets: Lipid Metabolism, Oxidative Stress & Inflammation

### 4.1 Herbs Modulating Lipid Metabolism

Dyslipidemia represents a major component of metabolic syndrome and frequently coexists with insulin resistance and impaired glucose regulation. An increasing amount of evidence suggests that many medicinal herbs provide lipid-modulating effects through mechanisms overlapping with antidiabetic pathways, particularly those involving AMP-activated protein kinase (AMPK) activation, peroxisome proliferator-activated receptor (PPAR $\alpha/\gamma$ ) signaling, and regulation of enzymes responsible for lipid synthesis and transport. Through these mechanisms, herbal bioactives may influence hepatic lipid metabolism, fatty acid oxidation, and intestinal lipid absorption simultaneously (Alam et al., 2022).

Fenugreek (*Trigonella foenum-graecum*) has been consistently reported to improve serum lipid profiles, including reductions in triglycerides and low-density lipoprotein (LDL) cholesterol alongside modest increases in high-density lipoprotein (HDL) cholesterol. These effects are largely attributed to its soluble fiber fraction and steroidal saponins, which may delay lipid absorption and alter bile acid metabolism, thereby contributing to improved lipid homeostasis (Qu, 2025).

Similarly, *Curcuma longa* and *Berberis aristata* have demonstrated lipid-lowering potential through modulation of AMPK and PPAR $\alpha$  pathways. Activation of these signaling mechanisms appears to suppress hepatic lipogenesis while enhancing lipid clearance (Hewlings & Kalman, 2017). Experimental studies further indicate that plants such as *Moringa oleifera*, *Momordica charantia*, and *Salacia reticulata* improve triglyceride and LDL-cholesterol concentrations, often alongside improvements in glucose metabolism, suggesting interconnected regulation of carbohydrate and lipid pathways (Chumark, et al;2008).

Green tea catechins have also been extensively investigated for their hypolipidemic properties. Proposed mechanisms include inhibition of lipogenic enzyme activity, enhancement of cholesterol excretion, and improvement of HDL functionality (Hursel & Westerterp-Plantenga, 2013). Although these findings are supported by both experimental and clinical observations, variability in study design and dosage continues to influence reported outcomes.

Cinnamon, a polyphenol rich herb, its polyphenols (such as proanthocyanidins and cinnamaldehyde) act as competitive inhibitors of enzymes that break down carbohydrates, thereby slowing glucose entry into the bloodstream hence showed lipid-lowering effects in animal models through reduced intestinal lipid absorption and inhibition of carbohydrate-digesting enzymes such as  $\alpha$ -glucosidase (Maierean et al., 2017).

Another well researched example is Garlic (*Allium sativum*) which has been reported to indicate reductions in serum cholesterol and triglycerides mediated partly through inhibition of HMG-CoA reductase activity and upregulation of hepatic LDL receptor expression (Ried et al, 2013).

Ginger (*Zingiber officinale*) has likewise demonstrated lipid-lowering effects in preclinical models, potentially through suppression of cholesterol biosynthesis and stimulation of fatty acid oxidation via AMPK signaling pathways; nevertheless, clinical trials specifically evaluating lipid outcomes remain limited (Choi, 2025; Mao et al., 2019).

Collectively, systematic reviews suggest that medicinal plant extracts can improve overall metabolic profiles, including lipid parameters. However, much of the available evidence derives from preclinical investigations, and large, well-controlled human trials assessing lipid endpoints are still comparatively scarce.

## 4.2 Herbs with Antioxidant & Anti-Inflammatory Mechanisms

Oxidative stress and inflammation play interconnected roles in the development of insulin resistance and atherogenic dyslipidemia. Excess production of reactive oxygen species (ROS) disrupts cellular signaling pathways involved in glucose and lipid metabolism, while persistent inflammatory activation further aggravates metabolic dysfunction. Consequently, phytochemicals capable of attenuating oxidative damage and inflammatory signaling may exert simultaneous benefits on glycemic regulation and lipid homeostasis.

A number of medicinal herbs are rich sources of polyphenols and flavonoids with established antioxidant activity. Compounds derived from *Curcuma longa*, *Thymus vulgaris*, and *Urtica dioica* have been shown to reduce ROS generation and suppress pro-inflammatory cytokines, thereby contributing to improvements in both glucose metabolism and lipid parameters (Panahi et al., 2015; Bnouham et al., 2002). Curcumin and related polyphenolic constituents, particularly those present in turmeric and tea, have demonstrated reductions in inflammatory mediators such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-6 (IL-6), effects that are associated with enhanced insulin sensitivity and improved lipid profiles in experimental and selected clinical studies.

Similarly, catechins from *Camellia sinensis*, along with bioactive compounds found in *Moringa oleifera* and *Cinnamomum verum*, exhibit antioxidant properties that support endothelial function, limit lipid peroxidation, and alleviate insulin resistance (Hursel & Westerterp-Plantenga, 2013; Mthiyane et al., 2022). These actions frequently converge with pathways involved in insulin signaling and lipid metabolism, emphasizing the multi-target nature of herbal interventions in metabolic disorders.

Anti-inflammatory activity has also been reported for herbs such as *Allium sativum*, *Momordica charantia*, and *Berberis aristata*, which reduce activation of nuclear factor- $\kappa$ B (NF- $\kappa$ B) and decrease circulating inflammatory cytokines including TNF- $\alpha$  and IL-6 (Ried et al., 2013; Basch et al., 2003). In addition, flavonoid-rich plants such as pomegranate and *Nigella sativa* possess strong free-radical scavenging capacity and influence redox-sensitive transcription factors linked to inflammatory responses, including IL-1 $\beta$  and high-sensitivity C-reactive protein (hsCRP). Evidence from human supplementation studies suggests that these effects may translate into measurable improvements in metabolic biomarkers.

Beyond glycemic control, attenuation of oxidative stress contributes to preservation of pancreatic  $\beta$ -cell integrity and prevents oxidative modification of low-density lipoprotein particles, thereby reducing endothelial dysfunction and vascular injury. These mechanisms provide a biological basis for the dual antidiabetic and antilipidemic actions attributed to antioxidant-rich medicinal herbs (Ansari et al; 2023).

## Sec-5 Mechanistic Targets of Medicinal Herbs in Metabolic Regulation

### 5.1 Herbs Enhancing Insulin Secretion

Progressive pancreatic  $\beta$ -cell dysfunction represents a defining feature in the pathogenesis of type 2 diabetes mellitus (T2DM), leading to impaired insulin secretion and loss of glucose homeostasis. Numerous medicinal plants have been investigated for their capacity to preserve  $\beta$ -cell integrity and enhance glucose-stimulated insulin release through diverse biochemical mechanisms.

Among the most extensively studied botanicals, *Trigonella foenum-graecum* (fenugreek) has demonstrated insulinotropic activity attributed primarily to 4-hydroxyisoleucine, an amino acid derivative capable of stimulating insulin secretion in a glucose-dependent manner, thereby minimizing hypoglycemic risk (Fuller & Stephens, 2015; Soriano et al., 2016; Neelakantan et al., 2014). Similarly, *Gymnema sylvestre* contains gymnemic acids that enhance insulin release while protecting pancreatic  $\beta$ -cells from

glucotoxic damage; although much of the mechanistic evidence originates from experimental models, preliminary clinical observations suggest therapeutic potential in T2DM management (Tiwari et al., 2014; Devangan et al., 2021).

Other traditionally used antidiabetic plants exert insulin-secretagogue effects through distinct bioactive constituents. *Momordica charantia* (bitter melon) contains compounds such as polypeptide-p and charantin that improve glycemic control and stimulate insulin secretion in both animal studies and selected clinical investigations (Dharani & Angappan, 2025; Basch et al., 2003). Extracts of *Salacia reticulata* and *Berberis aristata* have also demonstrated  $\beta$ -cell protective properties and enhancement of insulin output, although current evidence remains largely preclinical (Mazeed et al., 2021; Grover et al., 2002).

Emerging botanicals further expand the spectrum of insulin-modulating herbs. Bioactive compounds present in *Punica granatum* flowers, including punicalagins and oleanolic acid, have been shown to upregulate pancreatic Insulin-1 (Ins-1) gene expression, thereby promoting insulin secretion (Huang et al., 2024). *Ocimum sanctum* (Tulsi) enhances glucose-stimulated insulin secretion through modulation of intracellular calcium signaling within pancreatic islet cells (Hannan et al., 2023), while coumarin-rich extracts from *Aegle marmelos* reduce oxidative stress-induced  $\beta$ -cell apoptosis, supporting sustained insulin production (Singh et al., 2024).

Additional plants with supportive but less extensive evidence include *Urtica dioica*, which improves insulin secretion in diabetic animal models, and *Aloe vera*, whose antioxidant constituents appear to preserve  $\beta$ -cell function and enhance insulin release under experimental conditions (Noor et al., 2017).

Among these botanicals, *Urtica dioica* is particularly noteworthy due to its combined antioxidant and insulin-secretagogue properties, positioning it as a candidate for translational clinical evaluation. Collectively, medicinal herbs enhance insulin secretion through converging mechanisms that include protection against oxidative stress, stimulation of insulinotropic signaling pathways, and modulation of intracellular cascades such as PI3K/Akt and cAMP-dependent pathways. While fenugreek, bitter melon, and gymnema currently possess comparatively stronger human evidence, several emerging botanicals demonstrate promising mechanistic effects that warrant further clinical validation.

## 5.2 Herbs Improving Insulin Sensitivity

Restoration of peripheral insulin sensitivity is a central therapeutic objective in metabolic disorders. A growing body of evidence indicates that several medicinal herbs improve insulin responsiveness through modulation of intracellular signaling pathways, antioxidant activity, and attenuation of chronic inflammation. One of the most extensively investigated phytochemicals in this context is berberine, present in *Berberis aristata* and related species. Berberine acts as a potent activator of AMP-activated protein kinase (AMPK), a metabolic regulator that enhances glucose utilization by promoting translocation of glucose transporter-4 (GLUT4) to the cell membrane, thereby facilitating insulin-independent glucose uptake in skeletal muscle and adipose tissue (Yin et al., 2008; Yin et al., 2019). Activation of AMPK additionally suppresses hepatic gluconeogenesis, contributing to improved overall metabolic control.

Polyphenol-rich herbs also exert significant insulin-sensitizing effects. *Cinnamomum verum* (cinnamon) enhances insulin receptor phosphorylation and improves cellular glucose uptake, effects demonstrated in both experimental models and human studies reporting improvements in glycemic parameters (Khan et al., 2003). Similarly, *Curcuma longa* (turmeric) and its principal bioactive compound curcumin improve insulin sensitivity through multiple complementary mechanisms, including activation of AMPK, modulation of peroxisome proliferator-activated receptor- $\gamma$  (PPAR- $\gamma$ ), and inhibition of the pro-

inflammatory NF- $\kappa$ B signaling pathway, thereby alleviating inflammation-induced impairment of insulin signaling (Chuengsamarn et al., 2012; Panahi et al., 2021; Hewlings & Kalman, 2017).

Additional botanicals contribute through vascular and antioxidant mechanisms. *Allium sativum* (garlic) improves endothelial function and reduces oxidative stress, with clinical evidence indicating reductions in fasting insulin levels and improvements in HOMA-IR indices (Ried et al., 2013). Extracts of *Moringa oleifera* enhance glucose uptake and lipid metabolism via AMPK activation and increased GLUT4 expression in experimental studies, suggesting potential benefits for peripheral insulin action (Chumark et al., 2008).

Tea polyphenols also play an important role in metabolic regulation. Catechins from *Camellia sinensis*, particularly epigallocatechin gallate (EGCG), enhance insulin sensitivity by influencing PI3K/Akt signaling pathways, improving glucose uptake, and suppressing inflammatory mediators; supportive findings have been reported in clinical trials and meta-analyses (Hursel & Westerterp-Plantenga, 2013; Kim et al., 2011).

Other traditionally used medicinal plants, including *Ocimum sanctum* (Tulsi) and *Salacia reticulata*, have demonstrated improvements in insulin signaling and reductions in oxidative stress in animal studies, although robust human clinical validation remains limited (Prakash & Gupta, 2005).

Taken together, these herbs enhance insulin sensitivity through overlapping yet complementary mechanisms involving AMPK activation, modulation of PPAR signaling, improvement of glucose transporter activity, and suppression of inflammatory and oxidative pathways. Such multi-target actions highlight their potential role as adjunct strategies for managing insulin resistance and its associated cardiometabolic complications.

### 5.3 Herbs Inhibiting Carbohydrate Digestive Enzymes

An additional mechanism through which medicinal herbs attenuate postprandial hyperglycemia involves the inhibition of digestive enzymes responsible for carbohydrate breakdown, particularly  $\alpha$ -amylase and  $\alpha$ -glucosidase. By slowing enzymatic hydrolysis of dietary carbohydrates, these herbs delay glucose absorption and reduce post-meal glycemic excursions.

*Trigonella foenum-graecum* (fenugreek) seeds contain abundant soluble fiber and saponins that suppress the activity of carbohydrate-digesting enzymes, thereby moderating postprandial glucose responses (Ribes et al., 2022; Shibib et al., 2020). Similarly, *Momordica charantia* demonstrates significant  $\alpha$ -glucosidase inhibitory activity in both in vitro experiments and animal models, supporting its longstanding traditional application in glycemic management (Nguyen et al., 2021; Basch et al., 2020).

Polyphenolic compounds present in *Cinnamomum verum* (cinnamon) also contribute to enzyme inhibition, with experimental studies demonstrating suppression of carbohydrate digestive enzymes alongside clinical evidence showing improvements in postprandial glycemia (Maieran et al., 2017). In addition, berberine-containing plants and *Salacia reticulata* inhibit  $\alpha$ -glucosidase activity, reducing intestinal glucose absorption and limiting postprandial insulin surges, effects that may simultaneously benefit lipid metabolism (Yin et al., 2019; Jha et al., 2021). These mechanisms often operate in conjunction with enhanced insulin sensitivity and antioxidant activity, underscoring the multi-target metabolic actions of medicinal herbs.

### Modulation of Lipid Synthesis and Excretion

Beyond glycemic regulation, several medicinal plants influence lipid metabolism by targeting pathways involved in cholesterol synthesis and clearance. *Allium sativum* (garlic) contains allicin, which inhibits 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase—the rate-limiting enzyme in cholesterol

biosynthesis—thereby producing lipid-lowering effects comparable in mechanism to statin therapy (Ried et al., 2013).

Additionally, *Silybum marianum* (milk thistle) has been reported to enhance hepatic expression of low-density lipoprotein (LDL) receptors, facilitating increased clearance of circulating LDL cholesterol and contributing to improved lipid profiles (Huseini et al., 2006).

## 6. Discussion and Future Perspectives

A multitargeted approach for metabolic conditions is represented by herbal remedies that possess both antidiabetic and antilipidemic properties. A variety of herbs have combined effects on insulin secretion, insulin sensitivity, carbohydrate-lipid metabolism, and cellular stress, as illustrated in the sections and tables above. Such effects could lower the burden of polypharmacy, which is frequently observed in the treatment of diabetes and dyslipidemia.

For example, *Curcuma longa* increases insulin sensitivity, regulates lipid metabolism, and has strong antioxidant and anti-inflammatory properties, whereas *Trigonella foenum-graecum* has insulinotropic activity, inhibits enzymes that break down carbohydrates, and improves lipid profiles. *Berberis aristata* and *Momordica charantia* both have overlapping pathways that support lipid and glucose balance. These multi-target effects help manage metabolic syndrome by supporting the use of herbal formulations or combination medicines, aligning with the growing interest in functional foods and nutraceuticals (Kajimoto et al., 2002).

Despite encouraging mechanistic evidence, several important research gaps continue to limit the clinical translation of medicinal herbs for metabolic disorders. Many botanicals, including *Urtica dioica*, *Thymus vulgaris*, and *Salacia reticulata*, are supported predominantly by preclinical investigations, while human clinical trials remain limited in number and frequently involve small sample sizes. Furthermore, inconsistencies in extract preparation, bioactive compound characterization, and dosage standardization complicate comparisons across studies and hinder reproducibility of findings. Long-term safety evaluation and potential herb–drug interactions also remain insufficiently explored, particularly for herbs that influence multiple metabolic pathways simultaneously (Korani, B. et al., 2024).

Future investigations should therefore prioritize the following areas:

1. **Large-scale randomized controlled trials (RCTs)** to validate dual antidiabetic and antilipidemic effects in diverse populations.
2. **Human mechanistic studies** incorporating biomarkers related to insulin signaling, lipid metabolism, oxidative stress, and inflammatory pathways.
3. **Standardization of herbal extracts**, ensuring consistent concentrations of pharmacologically active constituents across studies.
4. **Combination-based therapeutic approaches**, examining synergistic interactions among herbs with complementary mechanisms of action.
5. **Comprehensive pharmacokinetic and safety assessments**, particularly for multi-herb formulations intended for long-term therapeutic use.

Overall, medicinal herbs represent a versatile multi-target strategy for metabolic regulation; however, translation from experimental findings to clinical recommendations requires rigorously designed and methodologically standardized research. Integration of herbs with demonstrated efficacy and safety into modern therapeutic frameworks may reduce reliance on multiple pharmacological agents, potentially minimizing adverse effects while improving patient adherence.

## 7. Conclusion

The present review demonstrates that medicinal herbs exert broad regulatory effects on metabolic disorders through multiple complementary mechanisms, including enhancement of insulin secretion, improvement of insulin sensitivity, inhibition of carbohydrate digestion, modulation of lipid metabolism, and attenuation of oxidative stress and inflammation. Botanicals such as *Trigonella foenum-graecum*, *Curcuma longa*, *Momordica charantia*, *Berberis aristata*, *Moringa oleifera*, and cinnamon exhibit overlapping mechanistic actions that collectively contribute to improved glycemic control and lipid homeostasis.

Although substantial experimental evidence supports these therapeutic potentials, clinical validation remains limited for many herbs, particularly with respect to optimal dosing strategies, long-term safety evaluation, and standardized extract formulations. Future research emphasizing well-designed randomized controlled trials, mechanistic human studies, and scientifically formulated multi-herb interventions will be essential for establishing evidence-based applications alongside conventional pharmacotherapy.

In conclusion, herbal interventions offer a promising multi-target approach for the integrated management of diabetes and dyslipidemia, with potential to enhance therapeutic efficacy, reduce treatment-related adverse effects, and improve patient compliance. Advancing from mechanistic understanding toward robust clinical validation will be critical for translating these botanicals into mainstream evidence-based therapeutic strategies.

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