

## Medicinal Herbs in the Management of Diabetes and Obesity: Molecular Mechanisms, Bioactive Phyto-constituents and Therapeutic Perspectives

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### Abstract

Diabetes mellitus and obesity are closely interconnected metabolic disorders characterized by insulin resistance, impaired glucose homeostasis, dysregulated lipid metabolism, chronic low-grade inflammation, oxidative stress, and alterations in energy balance. Numerous medicinal herbs have demonstrated antidiabetic and anti-obesity activities through multiple mechanisms, including inhibition of intestinal  $\alpha$ -amylase and  $\alpha$ -glucosidase, modulation of DPP-4, enhancement of insulin secretion, stimulation of IRS-1/PI3K/Akt signaling, GLUT4 translocation, activation of AMPK, modulation of PPARs, inhibition of adipogenesis and lipogenesis, stimulation of lipolysis and thermogenesis, and regulation of gut microbiota.

Important examples include *Momordica charantia*, *Gymnema sylvestre*, *Trigonella foenum-graecum*, *Cinnamomum spp.*, *Panax ginseng*, *Camellia sinensis*, *Gynostemma pentaphyllum*, *Phaseolus vulgaris*, and berberine-containing plants. This review emphasizes the molecular mechanisms underlying the dual antidiabetic and anti-obesity effects of medicinal herbs and discusses experimental and clinical evidence, limitations, safety considerations, and future perspectives.

**Keywords:** Diabetes, Obesity, Herbs, Management, Phyto-constituents

### Introduction

Diabetes mellitus and obesity represent major components of the global metabolic disease burden. Type 2 diabetes mellitus is characterized by progressive insulin resistance, impaired  $\beta$ -cell function, and abnormal hepatic and peripheral glucose metabolism, whereas obesity results from persistent energy imbalance accompanied by expansion and dysfunction of adipose tissue. These conditions are biologically interconnected because excess adiposity promotes inflammation, ectopic lipid accumulation and insulin resistance. Medicinal plants have historically been used for the management of diabetes and metabolic disorders, and modern pharmacological studies indicate that plant-derived compounds can influence several metabolic targets simultaneously rather than acting through a single pathway. (1-4)

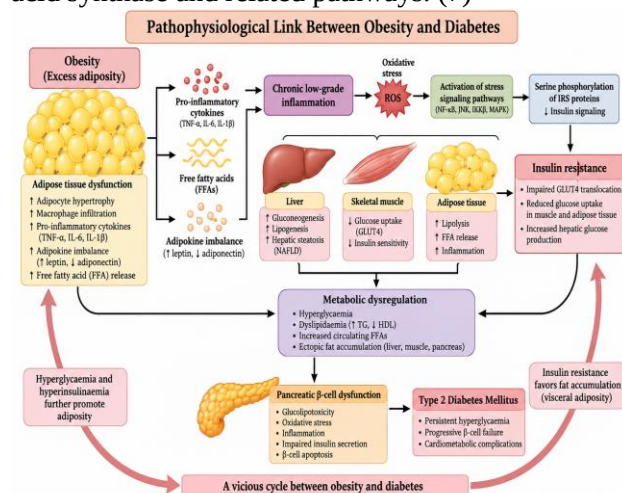
### Pathophysiological Link Between Diabetes and Obesity

Obesity is an important risk factor for T2DM because excessive adipose tissue accumulation promotes release of free fatty acids, inflammatory cytokines and adipokines. These mediators interfere with insulin signaling in liver, skeletal muscle and adipose tissue (4) At the molecular level, insulin normally activates the insulin receptor followed by IRS-1, PI3K and Akt signaling. Akt promotes GLUT4 translocation in skeletal muscle and adipose tissue, facilitating cellular glucose uptake. Insulin resistance can interfere with this pathway, reducing glucose disposal.

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AMPK represents another major metabolic regulator. AMPK activation promotes glucose uptake, fatty-acid oxidation, and energy expenditure while suppressing anabolic pathways such as fatty-acid synthesis (5,6). Consequently, AMPK has become an important target for both antidiabetic and anti-obesity natural products. Transcription factors including PPAR $\gamma$  and C/EBP $\alpha$  regulate adipocyte differentiation. Increased activation of these pathways promotes adipogenesis, whereas inhibition of adipogenic signaling can limit expansion of white adipose tissue. Plant-derived compounds have been shown experimentally to regulate PPAR $\gamma$ , C/EBP $\alpha$ , fatty-acid synthase and related pathways. (7)



**Fig. 1. Pathophysiological Link Between Diabetes and Obesity**

### Major Molecular Mechanisms of Herbal Antidiabetic and Anti-Obesity Activity

Medicinal herbs may act at multiple levels of glucose and lipid homeostasis. The major mechanisms include inhibition of carbohydrate-digesting enzymes, enhancement of insulin secretion, improvement of insulin signaling,

activation of AMPK, regulation of adipogenesis and lipogenesis, modulation of oxidative stress and inflammation, and alteration of gut microbiota.(8)

### Inhibition of $\alpha$ -Amylase and $\alpha$ -Glucosidase

Dietary starch is hydrolyzed by  $\alpha$ -amylase and subsequently converted to absorbable glucose by intestinal  $\alpha$ -glucosidases. Inhibition of these enzymes delays carbohydrate digestion and reduces postprandial glucose elevation. Flavonoids, phenolic acids, tannins and other plant metabolites have demonstrated inhibitory effects against these enzyme (9)

### Enhancement of Insulin Secretion and $\beta$ -Cell Protection

Several medicinal plants may increase insulin secretion from pancreatic  $\beta$ -cells or protect  $\beta$ -cells against oxidative and inflammatory injury. *Gymnema sylvestre* has been investigated clinically and experimentally for effects on glycemic control and pancreatic function. (10)

### IRS-1/PI3K/Akt/GLUT4 Signaling

The insulin signaling pathway is a major target for medicinal plants. Insulin receptor activation leads to IRS-1, PI3K and Akt signaling, followed by GLUT4 translocation and increased cellular glucose uptake. *Momordica charantia* and several phytochemicals have been reported to influence this pathway in experimental models. (11)

### AMPK: A Central Target Connecting Diabetes and Obesity

AMPK activation increases glucose uptake and fatty-acid oxidation while inhibiting anabolic pathways such as fatty-acid synthesis. Natural products including berberine, catechins and several saponins have been investigated as AMPK-modulating agents (12).

**Table 1. Important medicinal herbs used in the management of diabetes and obesity and their proposed mechanisms of action**

| S. No. | Medicinal herb                               | Major bioactive phytoconstituents                                                | Major antidiabetic mechanisms                                                                                            | Major anti-obesity/metabolic mechanisms                                                      |
|--------|----------------------------------------------|----------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|
| 1      | <i>Momordica charantia</i> L. (Bitter melon) | Charantin; cucurbitane-type triterpenoids; polypeptide-p; flavonoids; phenolics; | Inhibits $\alpha$ -amylase/ $\alpha$ -glucosidase; enhances glucose uptake; promotes GLUT4 translocation; modulates IRS- | Promotes fatty-acid metabolism; may activate AMPK; reduces lipogenesis; attenuates metabolic |

|   |                                           |                                                                              |                                                                                                                                                                 |                                                                                                                                             |
|---|-------------------------------------------|------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------|
|   |                                           | saponins                                                                     | 1/PI3K/Akt and AMPK; may reduce hepatic gluconeogenesis; antioxidant activity [11,13]                                                                           | inflammation and oxidative stress                                                                                                           |
| 2 | Gymnema sylvestre (Gurmar)                | Gymnemic acids; gymnemagenin; triterpenoid saponins; flavonoids              | Enhances insulin secretion; supports $\beta$ -cell function; reduces intestinal glucose absorption; improves glucose utilization and insulin sensitivity [10]   | May influence lipid metabolism and overall metabolic homeostasis                                                                            |
| 3 | Trigonella foenum-graecum L. (Fenugreek)  | 4-Hydroxyisoleucine; steroidal saponins; diosgenin; soluble fiber; alkaloids | Delays carbohydrate absorption; modulates carbohydrate-digesting enzymes; may enhance insulin secretion and improve insulin sensitivity [14]                    | Fiber promotes satiety; may reduce energy intake and improve lipid metabolism                                                               |
| 4 | Cinnamomum spp. (Cinnamon)                | Cinnamaldehyde; cinnamic acid; polyphenols; procyanidins                     | Enhances insulin signaling and glucose uptake; modulates GLUT4/AMPK; may inhibit carbohydrate-digesting enzymes and reduce oxidative stress [15,16]             | May influence AMPK and lipid metabolism; potentially reduces adipogenesis and improves insulin sensitivity                                  |
| 5 | Berberis spp./Coptis spp.                 | Berberine and related isoquinoline alkaloids                                 | Activates AMPK; improves PI3K/Akt signaling; promotes GLUT4-mediated glucose uptake; improves insulin sensitivity; may suppress hepatic gluconeogenesis [17,18] | Enhances fatty-acid oxidation; suppresses lipogenesis; modulates PPAR pathways; influences gut microbiota and metabolic inflammation        |
| 6 | Camellia sinensis (L.) Kuntze (Green tea) | EGCG; other catechins; caffeine                                              | May improve glucose metabolism and insulin sensitivity; modulates AMPK and oxidative-stress pathways [19,20]                                                    | Increases energy expenditure and fatty-acid oxidation; may inhibit adipogenesis and lipid accumulation; may influence thermogenesis [19,20] |
| 7 | Gynostemma pentaphyllum                   | Gypenosides and other dammarane-type saponins                                | Improves insulin sensitivity; activates AMPK; may enhance glucose utilization                                                                                   | Promotes fatty-acid oxidation; suppresses adipogenesis; may reduce abdominal fat and improve lipid metabolism [21]                          |
| 8 | Phaseolus                                 | Phaseolamin/ $\alpha$ -                                                      | Inhibits pancreatic $\alpha$ -                                                                                                                                  | Reduces carbohydrate                                                                                                                        |

|    |                                    |                                                                            |                                                                                                                |                                                                                                |
|----|------------------------------------|----------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|
|    | vulgaris L.<br>(White kidney bean) | amylase inhibitor;<br>lectins; polyphenols                                 | amylase; reduces starch digestion and postprandial glucose elevation                                           | availability/absorption and may support body-weight management [22]                            |
| 9  | Panax ginseng                      | Ginsenosides;<br>polysaccharides;<br>polyacetylenes;<br>phenolic compounds | May enhance insulin sensitivity and modulate PI3K/Akt and AMPK signaling; may improve glucose uptake           | May influence lipid metabolism, AMPK signaling and energy homeostasis; may reduce adipogenesis |
| 10 | Aegle marmelos                     | Marmelosin; aegeline;<br>flavonoids; tannins;<br>coumarins                 | May inhibit $\alpha$ -glucosidase; may enhance insulin action and reduce oxidative stress                      | Potential lipid-lowering and antioxidant effects; may improve metabolic dysfunction            |
| 11 | Syzygium cumini                    | Anthocyanins; ellagic acid; jamboline;<br>flavonoids; tannins              | May inhibit carbohydrate-digesting enzymes; supports glucose utilization and antioxidant defense               | May improve lipid profile and reduce oxidative stress associated with obesity                  |
| 12 | Curcuma longa L. (Turmeric)        | Curcumin;<br>demethoxycurcumin;<br>bisdemethoxycurcumin                    | Improves insulin sensitivity; modulates AMPK and PI3K/Akt; reduces oxidative stress and inflammatory signaling | Suppresses adipogenesis and lipogenesis; modulates AMPK and inflammatory pathways              |

**Table 2. Key molecular targets linking herbal mechanisms to diabetes and obesity**

| Molecular target/pathway | Effect of modulation      | Metabolic consequence                                                  | Representative herbs                            |
|--------------------------|---------------------------|------------------------------------------------------------------------|-------------------------------------------------|
| $\alpha$ -Amylase        | Inhibition                | Reduced starch digestion and postprandial glucose                      | M. charantia; P. vulgaris; fenugreek            |
| $\alpha$ -Glucosidase    | Inhibition                | Delayed intestinal glucose absorption                                  | M. charantia; cinnamon; A. marmelos             |
| DPP-4                    | Inhibition/modulation     | Prolonged incretin activity and improved glucose regulation            | Selected polyphenol- and alkaloid-rich herbs    |
| IRS-1/PI3K/Akt           | Activation/restoration    | Improved insulin signaling and glucose uptake                          | M. charantia; berberine; ginseng                |
| GLUT4                    | Increased translocation   | Increased skeletal-muscle and adipose glucose uptake                   | M. charantia; cinnamon; berberine               |
| AMPK                     | Activation                | Increased glucose uptake and fatty-acid oxidation; reduced lipogenesis | Berberine; green tea; G. pentaphyllum; turmeric |
| PPAR $\gamma$            | Modulation                | Regulation of adipocyte differentiation and insulin sensitivity        | Berberine; polyphenols                          |
| ACC/FAS                  | Inhibition/downregulation | Reduced fatty-acid synthesis                                           | Green tea; curcumin; polyphenols                |
| UCP1                     | Upregulation              | Increased thermogenesis and energy expenditure                         | Green tea and selected polyphenols              |

|                           |                        |                                                                 |                                             |
|---------------------------|------------------------|-----------------------------------------------------------------|---------------------------------------------|
| NF- $\kappa$ B/JNK/MAPK   | Suppression            | Reduced inflammation                                            | M. charantia; berberine; curcumin           |
| Oxidative-stress pathways | Antioxidant modulation | Protection of $\beta$ -cells and metabolic tissues              | M. charantia; cinnamon; turmeric; green tea |
| Gut microbiota            | Modulation             | Altered inflammation, energy metabolism and metabolic signaling | Berberine; green tea; polyphenols           |

### Integrated Mechanisms of Herbs Against Diabetes and Obesity

The diabetes–obesity axis is influenced by interconnected pathways involving carbohydrate digestion, insulin signaling, AMPK, PPARs, adipogenesis, lipogenesis, inflammation, oxidative stress and gut microbiota. Consequently, multi-target herbal preparations may influence several metabolic abnormalities simultaneously, although mechanistic activity observed in experimental models should not be equated automatically with clinical efficacy.(3-8,12)

### Role of Phytochemicals in the Diabetes–Obesity Axis

Polyphenols, alkaloids, saponins and triterpenoids constitute major classes of bioactive compounds investigated for metabolic effects. Their reported actions include modulation of AMPK, PI3K/Akt, GLUT4, PPAR $\gamma$ , inflammatory signaling and oxidative-stress pathways. (5,12,17,23)

### Gut Microbiota as an Emerging Mechanism

The gut microbiome can influence energy harvesting, intestinal barrier function, bile-acid metabolism and inflammation. Several plant-derived compounds, particularly berberine and polyphenols, have been investigated for their ability to modify gut microbial composition and microbial metabolites, providing a potential link between herbal therapy and metabolic homeostasis.(17,24)

### Oxidative Stress and Inflammation

Chronic hyperglycemia and obesity are associated with oxidative stress and low-grade inflammation. Important mediators include TNF- $\alpha$ , IL-6, NF- $\kappa$ B and JNK. Plant-derived phenolics, triterpenoids and alkaloids may attenuate these pathways while enhancing antioxidant defenses.(11,17,23)

### Clinical Evidence and Translational Challenges

Translation from experimental models to clinical practice is limited by differences in plant species, plant part, extraction procedure, phytochemical concentration, dose and study design. Clinical

meta-analyses for *Momordica charantia*, *Gymnema sylvestre*, cinnamon and green tea demonstrate potentially beneficial effects but also substantial heterogeneity.(10,13,15,19,20)

### 12. Safety and Herb–Drug Interactions

Medicinal plants should not automatically be considered risk-free. Potential concerns include hypoglycemia when combined with antidiabetic medicines, hepatic or renal adverse effects, herb–drug interactions, contamination, adulteration and variability in phytochemical content. Standardization and pharmacovigilance are therefore essential for clinical translation.(25)

### 13. Future Perspectives

Future research should emphasize authentication and standardization of plant material, chemical fingerprinting, pharmacokinetic characterization, multi-omics, network pharmacology, artificial intelligence-assisted target discovery and adequately powered randomized clinical trials. These approaches can help connect traditional medicinal knowledge with reproducible mechanism-based phytopharmaceutical development. (2,3,26)

### Conclusion

Medicinal herbs represent a diverse source of bioactive compounds capable of influencing multiple pathways involved in diabetes and obesity. Important mechanisms include inhibition of  $\alpha$ -amylase and  $\alpha$ -glucosidase, enhancement of insulin secretion, IRS-1/PI3K/Akt and GLUT4 signaling, AMPK activation, PPAR modulation, suppression of adipogenesis and lipogenesis, stimulation of fatty-acid oxidation, attenuation of oxidative stress and inflammation, and modulation of gut microbiota. However, differences in preparations and the variable quality of clinical evidence mean that individual herbal products should be evaluated on the basis of standardized composition, efficacy, safety and clinical evidence

rather than traditional use alone.  
(2,3,10,13,15,17,19)

## References

1. Newman DJ, Cragg GM. Natural products as sources of new drugs over the nearly four decades from 01/1981 to 09/2019. *J Nat Prod.* 2020;83(3):770-803. doi:10.1021/acs.jnatprod.9b01285.
2. Ríos JL, Francini F, Schinella GR. Natural products for the treatment of type 2 diabetes mellitus. *Planta Med.* 2015;81(12-13):975-994. doi:10.1055/s-0035-1544044.
3. Ríos JL, Bas E, Recio MC. Effects of natural compounds on inflammation and oxidative stress in metabolic disorders. *Pharmacol Res.* 2018;135:1-16.
4. Modak M, Dixit P, Londhe J, Ghaskadbi S, Devasagayam TPA. Indian herbs and herbal drugs used for the treatment of diabetes. *J Clin Biochem Nutr.* 2007;40(3):163-173. doi:10.3164/jcbrn.40.163.
5. Kim J, Yang G, Kim Y, Kim J, Ha J. AMPK activators: mechanisms of action and physiological activities. *Exp Mol Med.* 2016;48:e224. doi:10.1038/emmm.2016.16.
6. Boucher J, Kleinridders A, Kahn CR. Insulin receptor signaling in normal and insulin-resistant states. *Cold Spring Harb Perspect Biol.* 2014;6(1):a009191. doi:10.1101/cshperspect.a009191.
7. Rosen ED, Walkey CJ, Puigserver P, Spiegelman BM. Transcriptional regulation of adipogenesis. *Genes Dev.* 2000;14(11):1293-1307.
8. Tundis R, Loizzo MR, Menichini F. Natural products as  $\alpha$ -amylase and  $\alpha$ -glucosidase inhibitors and their potential in the treatment of diabetes. *Mini Rev Med Chem.* 2010;10(4):315-331.
9. Kwon YI, Apostolidis E, Shetty K. In vitro studies of the potential for alpha-amylase and alpha-glucosidase inhibition by selected foods. *J Agric Food Chem.* 2008;56(3):859-864.
10. Verma N, Shakya VK, Kumar A, et al. The effect of *Gymnema sylvestre* supplementation on glycemic control in type 2 diabetes patients: systematic review and meta-analysis. *Phytother Res.* 2021. doi:10.1002/ptr.7265.
11. Peter EL, Kasali FM, Deyno S, et al. *Momordica charantia* L. lowers elevated glycaemia in type 2 diabetes mellitus patients: systematic review and meta-analysis. *J Ethnopharmacol.* 2019;231:311-324.
12. Hardie DG. AMP-activated protein kinase: maintaining energy homeostasis at the cellular and whole body levels. *Annu Rev Nutr.* 2014;34:31-55.
13. Sridhar MG, Vinayagamoorathi R, Arul Suyambunathan V, Bobby Z, Selvaraj N. Bitter gourd (*Momordica charantia*) improves insulin sensitivity by increasing skeletal muscle insulin-stimulated glucose uptake. *Clin Nutr.* 2010;29(4):465-470.
14. Neelakantan N, Narayanan M, de Souza RJ, van Dam RM. Effect of fenugreek (*Trigonella foenum-graecum* L.) intake on glycemia: a meta-analysis of clinical trials. *Nutr J.* 2014;13:7.
15. Moridpour AH, Kavyani Z, Khosravi S, et al. The effect of cinnamon supplementation on glycemic control in patients with type 2 diabetes mellitus: an updated systematic review and dose-response meta-analysis of randomized controlled trials. *Phytother Res.* 2024;38:117-130.
16. Allen RW, Schwartzman E, Baker WL, Coleman CI, Phung OJ. Cinnamon use in type 2 diabetes: an updated systematic review and meta-analysis. *Ann Fam Med.* 2013;11(5):452-459.
17. Yin J, Xing H, Ye J. Efficacy of berberine in patients with type 2 diabetes mellitus. *Metabolism.* 2008;57(5):712-717.
18. Lan J, Zhao Y, Dong F, et al. Meta-analysis of the effect and safety of berberine in the treatment of type 2 diabetes mellitus, hyperlipemia and hypertension. *J Ethnopharmacol.* 2015;161:69-81.

19. Hursel R, Viechtbauer W, Dulloo AG, et al. The effects of green tea on weight loss and weight maintenance: a meta-analysis. *Int J Obes (Lond)*. 2009;33:956-961.
20. Tabrizi R, et al. The effects of green tea supplementation on obesity: systematic review and dose-response meta-analysis of randomized controlled trials. *Phytother Res*. 2020.
21. Park SH, et al. Antiobesity effect of *Gynostemma pentaphyllum* extract (actiponin): a randomized, double-blind, placebo-controlled trial. *Obesity (Silver Spring)*. 2014.
22. Onakpoya I, Posadzki P, Ernst E. The efficacy of *Phaseolus vulgaris* as a weight-loss supplement: a systematic review and meta-analysis of randomised clinical trials. *Br J Nutr*. 2011;106(9):1243-1251.
23. Kim Y, Keogh JB, Clifton PM. Polyphenols and obesity: evidence and mechanisms. *Nutrients*. 2016;8(4):231.
24. Anhê FF, Roy D, Pilon G, et al. A polyphenol-rich cranberry extract protects from diet-induced obesity, insulin resistance and intestinal inflammation in association with increased *Akkermansia* spp. population in the gut microbiota of mice. *Gut*. 2015;64(6):872-883.
25. Ekor M. The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. *Front Pharmacol*. 2014;4:177.
26. Vamathevan J, Clark D, Czodrowski P, et al. Applications of machine learning in drug discovery and development. *Nat Rev Drug Discov*. 2019;18:463-477.

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