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Review of Anti-Inflammatory Herbs as Adjunct Therapy for Type-2 Diabetes

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Abstract: *Type-2 diabetes mellitus is a chronic metabolic disorder characterized by insulin resistance, hyperglycemia, and low-grade systemic inflammation. Chronic inflammation contributes significantly to the progression of insulin resistance and β-cell dysfunction. Anti-inflammatory herbs, rich in bioactive compounds such as polyphenols, flavonoids, alkaloids, and terpenoids, have emerged as potential adjunct therapies to conventional antidiabetic drugs. These herbs can modulate inflammatory pathways, improve insulin sensitivity, and enhance glycemic control with minimal side effects. This review explores the role of anti-inflammatory herbs in T2DM management, their mechanisms of action, clinical evidence, and limitations.*

Keywords: Type-2 Diabetes, Anti-Inflammatory Herbs, Phytotherapy

I. INTRODUCTION

Type-2 diabetes mellitus is a global health concern, with increasing prevalence attributed to sedentary lifestyles, obesity, and dietary changes (American Diabetes Association, 2023). Chronic low-grade inflammation is recognized as a key contributor to insulin resistance and β-cell dysfunction in T2DM (Donath & Shoelson, 2011). Proinflammatory cytokines, including tumor necrosis factor-alpha interleukin-6 and C-reactive protein impair insulin signaling and exacerbate hyperglycemia (Hotamisligil, 2006). Targeting inflammation has therefore become a therapeutic strategy to improve insulin sensitivity and delay disease progression.

Herbs with anti-inflammatory properties have gained attention as adjunct therapies due to their ability to modulate inflammatory pathways, oxidative stress, and metabolic dysfunction. For centuries, traditional systems such as Ayurveda and Traditional Chinese Medicine have utilized herbs like *Curcuma longa Azadirachta indica Ocimum sanctum* and *Glycyrrhiza glabra* for managing metabolic disorders (Patel et al., 2021). Modern pharmacological studies have validated the anti-inflammatory, antioxidant, and insulin-sensitizing effects of these herbs, making them suitable candidates for adjunct therapy in T2DM.

Type-2 diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia, insulin resistance, and progressive β-cell dysfunction, affecting millions worldwide (American Diabetes Association, 2023). Beyond glucose dysregulation, chronic low-grade systemic inflammation has emerged as a critical factor in the pathogenesis and progression of T2DM. Elevated levels of proinflammatory cytokines such as tumor necrosis factor-alpha interleukin-6 and C-reactive protein interfere with insulin signaling pathways, impair glucose uptake in peripheral tissues, and exacerbate insulin resistance (Hotamisligil, 2006).

The inflammatory milieu not only contributes to metabolic derangements but also accelerates the development of diabetes-related complications, including cardiovascular disease, nephropathy, and neuropathy (Donath & Shoelson, 2011). Conventional antidiabetic therapies, such as metformin, sulfonylureas, and thiazolidinediones, primarily target hyperglycemia or insulin resistance; however, these drugs have limitations, including adverse effects, incomplete glycemic control, and limited ability to address underlying inflammation (Chatterjee et al., 2020).

In recent years, there has been growing interest in integrating anti-inflammatory herbal therapies as adjunct interventions in T2DM management. Traditional medicinal systems, such as Ayurveda and Traditional Chinese Medicine, have long utilized herbs with anti-inflammatory properties for metabolic disorders, and modern

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pharmacological research has provided scientific validation for these practices (Patel et al., 2021). Anti-inflammatory herbs contain bioactive compounds such as flavonoids, polyphenols, alkaloids, and terpenoids, which can modulate inflammatory signaling pathways, reduce oxidative stress, and improve insulin sensitivity (Suresh et al., 2019).

For example, Curcuma longa contains curcumin, a potent anti-inflammatory and antioxidant compound that inhibits NF-κB activation, suppresses proinflammatory cytokine production, and enhances glucose metabolism (Sharma et al., 2021). Similarly, Ocimum sanctum Azadirachta indica and Glycyrrhiza glabra have demonstrated anti-inflammatory effects that contribute to improved glycemic control and reduced insulin resistance (Jain et al., 2020).

The mechanisms by which anti-inflammatory herbs exert their beneficial effects are multifaceted. They involve inhibition of proinflammatory cytokines, suppression of oxidative stress, modulation of key transcription factors such as NF-κB, and activation of metabolic regulators like AMP-activated protein kinase and peroxisome proliferator-activated receptors which collectively improve insulin signaling and glucose uptake (Kumar et al., 2022). Importantly, polyherbal formulations, which combine multiple herbs, may produce synergistic effects, enhancing therapeutic outcomes and targeting multiple pathways simultaneously, a significant advantage over single-compound interventions (Jain et al., 2020).

Despite their potential, several challenges limit the clinical translation of anti-inflammatory herbs, including variability in active constituents, lack of standardized preparations, possible herb-drug interactions, and limited large-scale clinical trials (Suresh et al., 2019). Nonetheless, mounting preclinical and clinical evidence suggests that integrating anti-inflammatory herbs as adjunct therapy in T2DM management may improve glycemic control, reduce systemic inflammation, and mitigate complications, offering a complementary strategy to conventional pharmacotherapy. Continued research is essential to validate efficacy, determine optimal formulations and dosages, and establish safety guidelines for their use in diabetic populations.

MECHANISMS OF ACTION

Anti-inflammatory herbs improve glycemic control in T2DM through multiple mechanisms Anti-inflammatory herbs exert their beneficial effects in type-2 diabetes mellitus through multiple, interconnected mechanisms that target inflammation, oxidative stress, insulin resistance, and glucose metabolism. Chronic low-grade inflammation is a key contributor to insulin resistance and β-cell dysfunction, and anti-inflammatory herbs help modulate these pathological pathways. One major mechanism involves the inhibition of proinflammatory cytokines such as tumor necrosis factor-alpha interleukin-6 and C-reactive protein which are elevated in T2DM patients. Bioactive compounds like curcumin from Curcuma longa, quercetin from Ocimum sanctum, and berberine from Berberis aristata downregulate the expression of these cytokines, restoring insulin receptor signaling and improving glucose uptake in peripheral tissues (Jain et al., 2020).

Another key mechanism is the antioxidant activity of herbal compounds. Oxidative stress, characterized by excessive reactive oxygen species impairs insulin signaling and damages pancreatic β-cells, leading to hyperglycemia. Polyphenols, flavonoids, and saponins present in herbs scavenge ROS, reduce lipid peroxidation, and enhance the activity of endogenous antioxidant enzymes such as superoxide dismutase and catalase. This reduction in oxidative stress supports β-cell survival and function, thereby improving insulin secretion and sensitivity (Suresh et al., 2019).

Anti-inflammatory herbs also modulate key intracellular signaling pathways, including the nuclear factor kappa B pathway, AMP-activated protein kinase and peroxisome proliferator-activated receptor gamma. Inhibition of NF-κB by herbal bioactives suppresses transcription of proinflammatory genes, reducing systemic inflammation and preventing insulin resistance (Rao et al., 2018). Activation of AMPK by compounds such as berberine and cinnamaldehyde enhances glucose uptake, fatty acid oxidation, and energy homeostasis, thereby improving glycemic control. Additionally, several herbs act as natural PPARγ agonists, promoting adipocyte differentiation, enhancing glucose transport, and improving lipid metabolism, similar to conventional thiazolidinedione drugs but with fewer adverse effects (Kumar et al., 2022).

Furthermore, anti-inflammatory herbs can modulate gut microbiota, which has emerged as an important regulator of metabolic health. Polyphenols and other plant compounds promote the growth of beneficial bacteria and reduce the abundance of proinflammatory gut microbes, thereby reducing systemic inflammation and improving insulin sensitivity

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(Patel et al., 2021). Herbs also influence the secretion of adipokines, such as adiponectin and leptin, which play critical roles in glucose and lipid metabolism. Increased adiponectin levels, induced by herbal bioactives, enhance insulin sensitivity and reduce inflammation in peripheral tissues.

Collectively, these mechanisms highlight the multifaceted actions of anti-inflammatory herbs in T2DM management. By simultaneously targeting oxidative stress, inflammation, intracellular signaling pathways, and metabolic regulation, these herbs improve insulin sensitivity, preserve β-cell function, and support overall glycemic control. This multi-targeted approach provides a rationale for using anti-inflammatory herbs as adjunct therapies alongside conventional antidiabetic drugs, offering synergistic benefits while minimizing side effects. Future research focusing on molecular interactions and clinical validation will further elucidate the therapeutic potential of these herbs in comprehensive diabetes care.

Inhibition of Proinflammatory Cytokines: Bioactive compounds such as curcumin, quercetin, and berberine reduce the expression of TNF-α, IL-6, and CRP, thereby enhancing insulin receptor signaling and glucose uptake (Jain et al., 2020). Chronic low-grade inflammation is a hallmark of type-2 diabetes mellitus and plays a pivotal role in the development of insulin resistance and β-cell dysfunction. Elevated levels of proinflammatory cytokines such as tumor necrosis factor-alpha interleukin-6 and C-reactive protein have been closely associated with impaired insulin signaling, decreased glucose uptake in peripheral tissues, and increased hepatic gluconeogenesis (Hotamisligil, 2006).

These cytokines interfere with the insulin receptor substrate-1 and downstream signaling pathways, thereby exacerbating hyperglycemia and contributing to the progression of T2DM (Donath & Shoelson, 2011). Targeting these proinflammatory mediators has therefore emerged as a therapeutic strategy to enhance insulin sensitivity and improve glycemic control. Anti-inflammatory herbs, with their diverse bioactive compounds, have demonstrated significant potential in modulating these cytokines, making them valuable adjuncts to conventional antidiabetic therapies.

Herbs such as Curcuma longa Ocimum sanctum Azadirachta indica Glycyrrhiza glabra and Berberis aristata contain polyphenols, flavonoids, alkaloids, and terpenoids that exhibit potent anti-inflammatory activity. Curcumin, the primary bioactive compound of turmeric, has been extensively studied for its ability to inhibit the production and activity of TNF-α and IL-6 through suppression of nuclear factor kappa B signaling (Sharma et al., 2021).

Similarly, compounds such as eugenol in Ocimum sanctum and nimbidin in Azadirachta indica have been shown to downregulate proinflammatory cytokines and chemokines, reducing systemic inflammation and oxidative stress in diabetic conditions (Patel et al., 2021). By attenuating these cytokine levels, anti-inflammatory herbs restore insulin receptor function, improve glucose uptake in skeletal muscle and adipose tissue, and reduce hepatic glucose production, thereby enhancing overall insulin sensitivity.

Clinical studies support these molecular findings, demonstrating that supplementation with anti-inflammatory herbs can effectively lower circulating proinflammatory cytokines in T2DM patients. For example, randomized controlled trials have shown that turmeric supplementation significantly reduces serum TNF-α, IL-6, and CRP levels, accompanied by improvements in fasting blood glucose and HbA1c (Jain et al., 2020). Similarly, Ocimum sanctum and polyherbal formulations containing neem, gymnema, and pterocarpus extracts have been reported to decrease inflammatory markers and enhance insulin sensitivity in diabetic subjects over periods of 8–12 weeks (Suresh et al., 2019). These findings suggest that the anti-inflammatory effects of herbal interventions are closely linked to their ability to modulate proinflammatory cytokines, thereby supporting their role as adjunct therapy in T2DM management.

Despite promising outcomes, challenges such as variability in bioactive compound concentrations, standardization of herbal preparations, and potential herb-drug interactions must be addressed to ensure consistent efficacy and safety. Nonetheless, the ability of anti-inflammatory herbs to inhibit proinflammatory cytokines and improve insulin signaling positions them as a valuable complementary approach alongside conventional antidiabetic drugs. Continued research focusing on molecular mechanisms, optimized formulations, and well-designed clinical trials is essential to fully harness their therapeutic potential in managing type-2 diabetes.

Antioxidant Activity: Oxidative stress is closely linked to inflammation and insulin resistance. Herbal polyphenols scavenge reactive oxygen species, protect β-cells from oxidative damage, and support insulin secretion (Suresh et al., 2019). Oxidative stress plays a pivotal role in the pathophysiology of type-2 diabetes mellitus contributing to β-cell dysfunction, insulin resistance, and chronic inflammation. Elevated levels of reactive oxygen species disrupt cellular

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signaling, impair insulin receptor function, and promote lipid peroxidation, thereby exacerbating hyperglycemia and diabetic complications (Suresh et al., 2019).

Anti-inflammatory herbs are not only effective in modulating inflammatory pathways but also exhibit potent antioxidant activity, which is crucial for mitigating oxidative damage and restoring metabolic homeostasis. These herbs contain bioactive compounds such as flavonoids, polyphenols, alkaloids, terpenoids, and saponins, which act as free radical scavengers, metal chelators, and modulators of endogenous antioxidant enzymes (Jain et al., 2020).

The antioxidant activity of anti-inflammatory herbs enhances insulin sensitivity by protecting pancreatic β-cells from oxidative damage and improving glucose uptake in peripheral tissues. For instance, Curcuma longa contains curcumin, a polyphenolic compound that has been shown to increase the activity of endogenous antioxidant enzymes such as superoxide dismutase catalase and glutathione peroxidase while reducing lipid peroxidation and ROS levels in diabetic models (Sharma et al., 2021). Similarly, Ocimum sanctum exhibits strong free radical scavenging activity, reducing oxidative stress-induced damage in liver, muscle, and adipose tissue, which contributes to enhanced insulin receptor signaling and improved glucose homeostasis (Patel et al., 2021).

Polyherbal formulations combining multiple anti-inflammatory herbs have demonstrated synergistic antioxidant effects. For example, formulations containing Azadirachta indica, Gymnema sylvestre, and Pterocarpus marsupium significantly decrease ROS levels and increase antioxidant enzyme activity in both preclinical and clinical studies (Kumar et al., 2022). These antioxidant effects complement their anti-inflammatory properties, creating a dual mechanism that addresses both oxidative stress and inflammation two major drivers of insulin resistance in T2DM. The reduction of oxidative stress also indirectly enhances peroxisome proliferator-activated receptor gamma and AMP-activated protein kinase activity, further improving insulin sensitivity and glucose utilization in peripheral tissues (Rao et al., 2018).

Clinical evidence supports the role of antioxidant activity in improving metabolic outcomes in T2DM. Randomized controlled trials have shown that supplementation with antioxidant-rich herbs reduces fasting blood glucose, HbA1c, and oxidative stress markers, while simultaneously lowering proinflammatory cytokines such as TNF-α and IL-6 (Jain et al., 2020). Furthermore, these antioxidant effects are associated with reduced risk of diabetes-related complications, including neuropathy, nephropathy, and cardiovascular disease, highlighting the therapeutic potential of anti-inflammatory herbs beyond glycemic control.

The antioxidant activity of anti-inflammatory herbs plays a critical role in adjunctive therapy for T2DM by mitigating oxidative stress, protecting β-cells, enhancing insulin sensitivity, and complementing anti-inflammatory mechanisms. These effects underscore the importance of integrating antioxidant-rich herbs into comprehensive diabetes management strategies. Continued research on bioactive compounds, optimal dosages, and synergistic formulations is essential to maximize their therapeutic efficacy and safety in patients with type-2 diabetes.

Modulation of NF-κB Pathway: Many anti-inflammatory herbs inhibit nuclear factor kappa B a transcription factor that regulates proinflammatory gene expression, thereby reducing systemic inflammation and improving insulin sensitivity (Rao et al., 2018). Chronic low-grade inflammation is a central feature of type-2 diabetes mellitus contributing significantly to insulin resistance, β-cell dysfunction, and vascular complications. One of the key molecular mediators of inflammation in T2DM is the nuclear factor kappa B pathway, a transcription factor that regulates the expression of numerous proinflammatory cytokines, chemokines, and adhesion molecules. In hyperglycemic and lipotoxic conditions, NF-κB becomes persistently activated, leading to elevated levels of tumor necrosis factor-alpha interleukin-6 and C-reactive protein all of which interfere with insulin receptor signaling and exacerbate metabolic dysfunction (Hotamisligil, 2006; Donath & Shoelson, 2011). Targeting NF-κB signaling has therefore emerged as a promising therapeutic strategy to mitigate inflammation-induced insulin resistance.

Anti-inflammatory herbs have demonstrated potent modulatory effects on the NF-κB pathway, positioning them as valuable adjuncts to conventional antidiabetic therapies. Bioactive compounds present in herbs such as Curcuma longa Ocimum sanctum (eugenol, ursolic acid), Azadirachta indica and Glycyrrhiza glabra can inhibit NF-κB activation through multiple mechanisms. Curcumin, for instance, suppresses the phosphorylation and degradation of the inhibitory protein IκBα, preventing NF-κB translocation into the nucleus and subsequent transcription of proinflammatory genes

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(Jain et al., 2020). Similarly, eugenol and ursolic acid from Ocimum sanctum reduce NF-κB activation and cytokine production, thereby improving insulin sensitivity in adipose tissue and skeletal muscle (Patel et al., 2021).

The modulation of NF-κB by anti-inflammatory herbs not only decreases systemic inflammation but also indirectly enhances insulin signaling. By lowering TNF-α and IL-6 levels, these herbal compounds restore the phosphorylation of insulin receptor substrate-1 and activate the phosphatidylinositol 3-kinase pathway, facilitating glucose uptake in peripheral tissues (Kumar et al., 2022). In addition, NF-κB inhibition reduces oxidative stress and lipid peroxidation, further protecting pancreatic β-cells from damage and supporting endogenous insulin secretion. This dual effect on inflammation and oxidative stress underscores the potential of herbal NF-κB modulators in improving glycemic control and preventing diabetes-associated complications.

Clinical studies support these molecular insights. Supplementation with curcumin in T2DM patients has been shown to reduce circulating levels of NF-κB and proinflammatory cytokines, accompanied by significant improvements in fasting blood glucose, HbA1c, and HOMA-IR values (Sharma et al., 2021). Polyherbal formulations containing combinations of NF-κB-modulating herbs, such as Azadirachta indica, Gymnema sylvestre, and Pterocarpus marsupium, have demonstrated synergistic anti-inflammatory and insulin-sensitizing effects, further highlighting the clinical relevance of NF-κB pathway modulation (Jain et al., 2020).

The modulation of the NF-κB pathway represents a key mechanism by which anti-inflammatory herbs exert their beneficial effects in T2DM. By inhibiting NF-κB activation, reducing proinflammatory cytokine production, and restoring insulin signaling, these herbs provide a multi-targeted, safe, and effective adjunctive strategy for managing hyperglycemia and associated complications. Continued research into the precise molecular interactions and long-term clinical efficacy of NF-κB-targeting herbal interventions is essential to optimize their therapeutic potential in diabetes management.

ACTIVATION OF AMPK AND PPAR PATHWAYS

Certain herbs activate AMP-activated protein kinase and peroxisome proliferator-activated receptors (PPARα and PPARγ), enhancing glucose uptake, lipid metabolism, and insulin sensitivity (Kumar et al., 2022).

CLINICAL EVIDENCE

Clinical trials have demonstrated the efficacy of anti-inflammatory herbs in T2DM management:

A randomized controlled trial reported that supplementation with *Curcuma longa* extract significantly reduced HbA1c, fasting blood glucose, and serum TNF-α levels in T2DM patients (Sharma et al., 2021).

Ocimum sanctum supplementation improved glycemic indices and decreased proinflammatory markers in T2DM subjects over 12 weeks (Patel et al., 2021).

Polyherbal formulations containing anti-inflammatory herbs, such as *Azadirachta indica*, *Gymnema sylvestre*, and *Pterocarpus marsupium*, have shown synergistic effects in reducing insulin resistance and systemic inflammation (Jain et al., 2020). These findings suggest that anti-inflammatory herbs can serve as effective adjuncts to conventional therapies, particularly in patients with persistent inflammation and poor glycemic control.

CHALLENGES AND LIMITATIONS

Despite promising results, several challenges remain:

Standardization: Variability in herb species, preparation methods, and bioactive compound concentrations can affect efficacy (Suresh et al., 2019).

Safety and Herb-Drug Interactions: Potential interactions with conventional antidiabetic medications may lead to hypoglycemia or other adverse effects (Jain et al., 2020).

Limited Large-Scale Trials: Most studies are small-scale; further randomized controlled trials are needed to establish clinical guidelines for dosage and duration.

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II. CONCLUSION

Anti-inflammatory herbs represent a promising adjunct therapy for managing T2DM by targeting systemic inflammation, oxidative stress, and insulin resistance. Herbs such as *Curcuma longa*, *Ocimum sanctum*, and *Azadirachta indica* demonstrate both molecular and clinical efficacy in improving glycemic control. While challenges regarding standardization, safety, and large-scale validation remain, integration of anti-inflammatory herbs into T2DM management could complement conventional therapies, offering holistic and multi-targeted benefits. Future research should focus on elucidating molecular mechanisms, optimizing formulations, and conducting well-designed clinical trials to ensure efficacy and safety.

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