International Journal of Advanced Research and Multidisciplinary Trends (IJARMT)
An International Open Access, Peer-Reviewed Refereed Journal
Impact Factor: 6.4 Website: https://ijarmt.com ISSN No.: 3048-9458

PHARMACODYNAMIC EVALUATION OF THE SYNERGISTIC ANTIDIABETIC EFFECT OF OCIMUM SANCTUM IN COMBINATION WITH STANDARD ORAL HYPOGLYCEMIC AGENTS

Vyas Kishor Revashankar

Ph.D Research Scholar, Department of Pharmacy, Shri Jagdishprasad Jhabarmal Tibrewala University, Jhunjhunu Rajasthan,India

Prof. Dr. Rakesh Kumar Jat

Principal & PhD Research Guide, Department of Pharmacy, Shri Jagdishprasad Jhabarmal Tibrewala University, Jhunjhunu Rajasthan, India

Diabetes mellitus remains one of the most challenging metabolic disorders globally, requiring long-term therapeutic strategies to maintain glycemic control and prevent complications. Although conventional oral hypoglycemic agents (OHAs) such as metformin, glibenclamide, and pioglitazone remain the mainstay of treatment, limitations such as drug resistance, gastrointestinal side effects, and oxidative stress necessitate the search for safer and more effective complementary approaches. Ocimum sanctum (Tulsi), a well-known medicinal plant in Ayurveda, possesses documented antidiabetic, antioxidant, and immunomodulatory properties. The present study aims to evaluate the pharmacodynamic synergism between Ocimum sanctum extract and standard OHAs in improving glycemic regulation. bA synergistic herbal–allopathic formulation was developed and administered to diabetic animal models induced using streptozotocin. Pharmacodynamic parameters including fasting blood glucose, postprandial glucose, serum insulin, HbA1c, lipid profile, and oxidative stress markers (MDA, SOD, CAT) were evaluated across various treatment groups. Histopathological examination of pancreatic tissue was conducted to assess β-cell protection and regeneration. The results demonstrated that the combination of Ocimum sanctum with conventional antidiabetic drugs produced significantly greater glycemic control compared to monotherapy. Marked reductions in fasting glucose, improved insulin sensitivity, restoration of lipid levels, and enhanced antioxidant status were observed. Histological analysis revealed improved pancreatic islet architecture and reduced cellular degeneration. The synergistic formulation exhibited superior efficacy while potentially lowering required doses of standard OHAs. This study concludes that Ocimum sanctum enhances the pharmacodynamic actions of conventional hypoglycemic agents and holds substantial promise for developing safer, more effective, and holistic antidiabetic therapies.

Keywords: Ocimum sanctum; synergistic formulation; pharmacodynamics; antidiabetic activity; oral hypoglycemic agents; metformin; streptozotocin; oxidative stress; β-cell protection; glycemic control.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) represents one of the most significant global health challenges, affecting over 537 million adults worldwide and contributing to approximately 6.7

International Journal of Advanced Research and Multidisciplinary Trends (IJARMT)
An International Open Access, Peer-Reviewed Refereed Journal
Impact Factor: 6.4 Website: https://ijarmt.com ISSN No.: 3048-9458

million deaths annually [1]. While conventional oral hypoglycemic agents such as metformin, sulfonylureas, and dipeptidyl peptidase-4 inhibitors provide effective glycemic control, their prolonged use is frequently associated with adverse effects including gastrointestinal disturbances, weight gain, and hypoglycemic episodes [2]. These limitations have prompted extensive research into complementary and alternative medicine approaches, particularly botanical interventions that may offer synergistic benefits when combined with standard antidiabetic therapies [3].

Ocimum sanctum (Linn), commonly known as Holy Basil or Tulsi, is a fragrant herbaceous plant belonging to the Lamiaceae family, widely cultivated in north-central India and other tropical regions [4]. This plant has been extensively documented in traditional medicine systems, particularly Ayurveda and Traditional Chinese Medicine, for its therapeutic properties spanning antimicrobial, anti-inflammatory, antioxidant, and antidiabetic domains [4]. The growing body of empirical evidence supports the pharmacodynamic potential of O. sanctum as an adjunctive antidiabetic agent, with multiple studies demonstrating its efficacy in improving glycemic control through diverse molecular mechanisms [1]. Recent investigations have revealed that O. sanctum exhibits antidiabetic properties comparable to or exceeding those of conventional agents, with IC_{50} values indicating potent enzymatic inhibition [5].

The rationale for investigating combination therapy of O. sanctum with standard oral hypoglycemic agents stems from several compelling factors. First, herbal preparations often demonstrate multitarget activity, addressing multiple pathophysiological pathways implicated in diabetes pathogenesis, whereas conventional drugs typically target single mechanisms [3]. Second, preliminary evidence suggests that certain herbal-drug combinations produce synergistic rather than merely additive effects, potentially allowing dose reduction of conventional agents while maintaining or enhancing therapeutic outcomes [6]. Third, the relatively mild adverse effect profile of O. sanctum, combined with its cultural acceptance in traditional medicine systems, makes it an attractive candidate for adjunctive therapy [4]. Finally, the prevalence of treatment-resistant hyperglycemia and the increasing incidence of adverse drug reactions underscore the clinical need for combination strategies that optimize glycemic control while minimizing toxicity [2].

This comprehensive review and original research paper evaluates the pharmacodynamic interactions between O. sanctum and standard oral hypoglycemic agents, examining the mechanistic basis for synergistic antidiabetic effects, pharmacokinetic considerations, and clinical implications for integrated diabetes management. Through systematic analysis of in vitro enzyme inhibition assays, animal model studies, and limited human clinical trials, we demonstrate that O. sanctum augments the antidiabetic efficacy of metformin, glibenclamide, and other first-line antidiabetic agents while potentially reducing systemic toxicity through enhanced antioxidant and hepatoprotective mechanisms.

PHARMACODYNAMIC MECHANISMS OF OCIMUM SANCTUM

Ocimum sanctum exerts its antidiabetic effects through multiple complementary mechanisms, each contributing to improved glucose homeostasis through distinct molecular pathways (Figure 1). The primary bioactive constituents responsible for these effects include eugenol,

International Journal of Advanced Research and Multidisciplinary Trends (IJARMT)
An International Open Access, Peer-Reviewed Refereed Journal
Impact Factor: 6.4 Website: https://ijarmt.com ISSN No.: 3048-9458

ursolic acid, oleanolic acid, rosmarinic acid, and various polyphenolic compounds including quercetin and kaempferol [1]. These compounds demonstrate synergistic action within the plant matrix, a phenomenon termed the "entourage effect," wherein combined constituents produce greater therapeutic activity than isolated individual components [3].

A. Carbohydrate-Metabolizing Enzyme Inhibition

One of the most extensively characterized mechanisms of O. sanctum's antidiabetic activity involves the inhibition of carbohydrate-hydrolyzing enzymes, specifically α-amylase and α-glucosidase [5]. These enzymes catalyze the degradation of complex carbohydrates and disaccharides into glucose in the small intestine. By inhibiting their enzymatic activity, O. sanctum reduces postprandial glucose absorption, thereby attenuating hyperglycemic spikes following meal consumption [5]. Recent studies have established a strong positive correlation ($R^2 = 0.994$) between the total phenolic content of O. sanctum extracts and their α-amylase inhibitory capacity, indicating that phenolic compounds serve as primary active constituents [5]. Methanol extracts of dried O. sanctum leaves demonstrated the highest inhibitory activity, achieving 47.0% inhibition of α-amylase at standard concentrations, with IC_{50} values significantly lower than some conventional antidiabetic agents [5].

The mechanism of enzyme inhibition appears to be primarily noncompetitive, wherein bioactive constituents interact with allosteric sites on the enzyme rather than occupying the active site directly [5]. This noncompetitive inhibition pattern suggests that O. sanctum-derived compounds may exhibit additive effects when combined with hypoglycemic agents that employ alternative mechanisms, supporting the theoretical basis for synergistic combination therapy [6].

B. Insulin Secretion and Pancreatic β-Cell Function

Several lines of evidence indicate that O. sanctum enhances endogenous insulin secretion through direct effects on pancreatic β-cell function. Animal studies employing alloxan-induced diabetes models demonstrated that O. sanctum treatment resulted in dose-dependent improvements in plasma insulin levels and pancreatic histomorphology [1]. At the highest effective dose (900 mg/kg), O. sanctum treatment produced statistically significant ($p < 0.05$) restoration of pancreatic tissue architecture and enhancement of β-cell insulin granule density compared to untreated diabetic controls [1]. The mechanism underlying this effect appears to involve eugenol-mediated modulation of ATP-sensitive potassium channels and calcium-dependent insulin exocytosis pathways, similar to sulfonylurea mechanism but through distinct biochemical targets [1].

Furthermore, O. sanctum exhibits cytoprotective effects specifically targeting pancreatic β-cells through antioxidant mechanisms, preventing the nitrosative and oxidative stress-induced loss of β-cell mass characteristic of both Type 1 and Type 2 diabetes progression [4]. This dual action—simultaneous enhancement of insulin secretion and protection against β-cell loss—positions O. sanctum as particularly valuable in combination therapy, where it may potentiate the glucose-stimulated insulin secretion triggered by sulfonylurea or meglitinide agents while simultaneously preventing the progressive β-cell dysfunction that limits long-term efficacy of these drug classes [3].

International Journal of Advanced Research and Multidisciplinary Trends (IJARMT)
An International Open Access, Peer-Reviewed Refereed Journal
Impact Factor: 6.4 Website: https://ijarmt.com ISSN No.: 3048-9458

C. Insulin Sensitivity and Hepatic Glucose Metabolism

Ursolic acid and oleanolic acid, major pentacyclic triterpenoids present in O. sanctum, have been demonstrated to enhance peripheral insulin sensitivity through multiple mechanisms [1]. These compounds improve glucose transporter 4 (GLUT4) translocation to the cell membrane, enhancing glucose uptake in skeletal muscle and adipose tissue [3]. Additionally, they inhibit hepatic gluconeogenesis and promote hepatic glycogenesis, the latter having been demonstrated in experimental models as a dose-dependent increase in liver glycogen content by 31.8-45.2% compared to untreated diabetic controls [1]. This hepatic effect directly addresses one of the fundamental pathophysiological defects in Type 2 diabetes—excessive endogenous glucose production accounting for 90% of fasting hyperglycemia—through a mechanism distinct from biguanide inhibition of complex I of the mitochondrial electron transport chain [6].

Notably, O. sanctum's capacity to enhance insulin sensitivity appears independent of weight reduction, as clinical and animal studies reported decreased body weight was not statistically significant despite substantial improvements in glycemic parameters [1]. This suggests that the hepatic and peripheral insulin-sensitizing effects occur through direct molecular actions rather than through weight-dependent mechanisms, potentially offering clinical advantage in patients with limited capacity for lifestyle-based weight loss [1].

D. Antioxidant and Anti-inflammatory Effects

Oxidative stress and chronic low-grade inflammation represent fundamental pathophysiological processes linking insulin resistance to pancreatic β-cell dysfunction in Type 2 diabetes [3]. O. sanctum extracts demonstrate robust antioxidant capacity through both enzymatic and non-enzymatic mechanisms, significantly upregulating superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) activities while simultaneously reducing hepatic lipid peroxidation by 37-42%[1]. The rosmarinic acid and quercetin content of O. sanctum accounts for a substantial portion of this antioxidant effect through direct radical scavenging and via metal chelation mechanisms [4].

The anti-inflammatory properties of O. sanctum involve inhibition of nuclear factor-kappa B (NF-κB) pathway activation, thereby reducing systemic production of pro-inflammatory cytokines including tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP)[4]. By ameliorating the inflammatory environment underlying insulin resistance, O. sanctum addresses a fundamental pathophysiological mechanism distinct from the single-target action of most oral hypoglycemic agents. This multi-level antioxidant and anti-inflammatory action becomes particularly relevant when combined with metformin, which has been shown to independently exhibit antioxidant properties, potentially yielding enhanced reduction of oxidative stress markers when used in combination therapy [6].

SYNERGISTIC EFFECTS IN COMBINATION THERAPY

The term "synergy" in pharmacology describes a situation wherein the combined effect of two or more agents exceeds the sum of their individual effects, representing a greater-than-additive response [2]. Multiple studies examining herbal-drug combinations have documented

International Journal of Advanced Research and Multidisciplinary Trends (IJARMT)
An International Open Access, Peer-Reviewed Refereed Journal
Impact Factor: 6.4 Website: https://ijarmt.com ISSN No.: 3048-9458

synergistic interactions with standard antidiabetic agents, though the mechanistic basis for such interactions remains incompletely characterized.

A. Ocimum sanctum Combined with Metformin

Metformin, a biguanide compound and first-line agent for Type 2 diabetes management, exerts its primary antidiabetic effect through activation of AMP-activated protein kinase (AMPK), leading to enhanced glycolysis and reduced hepatic gluconeogenesis [6]. Given that O. sanctum operates through mechanistically distinct pathways—carbohydrate enzyme inhibition, enhanced insulin secretion, and improved insulin sensitivity—theoretical basis exists for synergistic interaction. A clinical trial examining the combined effect of herbal formulations containing O. sanctum with reduced-dose metformin (50% standard dose) demonstrated a significantly greater reduction in fasting blood glucose (32.4% reduction) compared to full-dose metformin monotherapy (28.1% reduction), suggesting a synergistic response [3].

The mechanistic basis for O. sanctum-metformin synergy may involve complementary effects on multiple glucose metabolism pathways: metformin primarily addresses hepatic glucose overproduction, while O. sanctum enhances peripheral glucose utilization and reduces intestinal glucose absorption. Additionally, the enhanced antioxidant activity of the combination may reduce metformin-associated side effects, particularly gastrointestinal toxicity mediated through oxidative stress mechanisms [6]. Furthermore, preliminary evidence suggests that O. sanctum may enhance metformin's bioavailability through inhibition of P-glycoprotein efflux transporter, though this hypothesis requires further investigation in controlled pharmacokinetic studies [3].

B. Ocimum sanctum Combined with Sulfonylureas

Sulfonylurea agents (glibenclamide, glipizide, gliclazide) enhance insulin secretion through closure of ATP-sensitive potassium channels in pancreatic β-cell membranes, leading to depolarization and calcium-dependent insulin exocytosis [3]. The combination of O. sanctum with sulfonylureas presents both therapeutic opportunity and safety consideration. On the beneficial side, O. sanctum's capacity to regenerate and protect pancreatic β-cell mass through antioxidant mechanisms may mitigate the progressive β-cell exhaustion and secondary failure typically observed during prolonged sulfonylurea monotherapy [3]. Studies employing glibenclamide with fenugreek extract (a plant with mechanistically similar antidiabetic properties to O. sanctum) demonstrated a 43% reduction in glycosylated hemoglobin compared to glibenclamide monotherapy, accompanied by enhanced antioxidant enzyme activity [6].

However, the combination of O. sanctum with sulfonylureas requires careful clinical monitoring for hypoglycemia, as both agents independently enhance insulin secretion through partially overlapping mechanisms [3]. A case report documented severe hypoglycemia in a patient receiving concurrent ginseng (another herbal antidiabetic agent) and sulfonylurea monotherapy, emphasizing the necessity for dose adjustment and intensive glucose monitoring when herbal agents are combined with insulin secretagogues [3]. Therefore, while the combination demonstrates enhanced antidiabetic efficacy, clinical implementation requires dose reduction of the sulfonylurea component and patient education regarding hypoglycemia recognition and management [3].

International Journal of Advanced Research and Multidisciplinary Trends (IJARMT)
An International Open Access, Peer-Reviewed Refereed Journal
Impact Factor: 6.4 Website: https://ijarmt.com ISSN No.: 3048-9458

C. Ocimum sanctum Combined with DPP-4 Inhibitors and Thiazolidinediones

Dipeptidyl peptidase-4 (DPP-4) inhibitors enhance incretin-mediated insulin secretion by inhibiting degradation of glucagon-like peptide-1 (GLP-1), whereas thiazolidinediones enhance insulin sensitivity through peroxisome proliferator-activated receptor-gamma (PPAR-γ) activation [2]. Both drug classes operate through distinct mechanisms from O. sanctum's primary antidiabetic pathways. Theoretical considerations suggest that O. sanctum combination with these agents would produce additive rather than synergistic effects, though clinical trial data specifically examining such combinations remains limited [3]. The antioxidant properties of O. sanctum may offer additional hepatoprotective benefit when combined with thiazolidinediones, which carry risk of hepatotoxicity in susceptible individuals [2]. Additionally, O. sanctum's reported capacity to enhance insulin sensitivity through GLUT4 translocation may provide complementary effects to thiazolidinedione PPAR-γ activation [3].

CLINICAL EVIDENCE AND PHARMACOKINETIC CONSIDERATIONS

A. Human Clinical Trial Data

Despite the substantial preclinical evidence supporting O. sanctum's antidiabetic efficacy, the paucity of high-quality human clinical trials represents a significant limitation in the current evidence base. A limited number of clinical trials have directly examined O. sanctum's effects in diabetic patients, with most studies employing relatively small sample sizes, limited control conditions, and heterogeneous outcome measures [1]. One notable clinical trial examining 400 mg daily of O. sanctum extract in 40 patients with Type 2 diabetes demonstrated a statistically significant reduction in fasting blood glucose (48.2 mg/dL reduction, $p < 0.05$) and glycosylated hemoglobin (-1.2%, $p < 0.05$) over an 8-week intervention period [4]. However, the absence of a concurrent active control group limits interpretation regarding relative efficacy compared to standard agents.

A cross-sectional study analyzing 739 Thai individuals found that those utilizing O. sanctum (or other herbal agents) in combination with metformin at 500 mg/day were approximately 2.9 times more likely to achieve good glycemic control (adjusted odds ratio = 2.921, 95% CI = 1.227–6.952, $p = 0.015$) compared to metformin monotherapy [3]. While this observational study design carries inherent limitations regarding confounding variable control, the magnitude of the association and statistical significance suggest meaningful clinical benefit warranting further investigation through randomized controlled trials [3].

B. Pharmacokinetic Interactions

The potential for pharmacokinetic interactions between O. sanctum and standard antidiabetic agents must be carefully evaluated for safe clinical implementation. Preliminary evidence from animal pharmacokinetic studies examining garlic (a botanical agent with mechanistically similar properties to O. sanctum) in combination with metformin demonstrated increased peak plasma concentration (Cmax) and area under the concentration-time curve (AUC) of metformin, raising the possibility of enhanced bioavailability [6]. If such interactions occur with O. sanctum, they could either enhance therapeutic efficacy (beneficial interaction) or necessitate dose reduction of the conventional agent to avoid toxicity (adverse interaction) [2].

International Journal of Advanced Research and Multidisciplinary Trends (IJARMT)
An International Open Access, Peer-Reviewed Refereed Journal
Impact Factor: 6.4 Website: https://ijarmt.com ISSN No.: 3048-9458

The bioactive constituents of O. sanctum, particularly ursolic acid and oleanolic acid, are extensively metabolized via hepatic cytochrome P450 oxidation and phase II conjugation reactions, the same enzymatic systems responsible for metabolism of many antidiabetic agents [1]. Although direct inhibition of CYP3A4 or other major metabolic enzymes has not been definitively demonstrated for O. sanctum extracts, the potential for competitive metabolic inhibition exists, particularly at high doses or with prolonged use [3]. Additionally, O. sanctum's reported inhibition of P-glycoprotein efflux transporter could theoretically enhance intracellular penetration of P-glycoprotein substrate drugs, potentially increasing their systemic exposure [3].

These theoretical pharmacokinetic considerations underscore the critical need for prospective pharmacokinetic studies specifically examining the temporal profiles of both O. sanctum constituents and standard antidiabetic agents when administered in combination [2]. Such studies should employ simultaneous plasma sampling of both herbal and conventional drug components, enabling quantitative assessment of potential interactions and optimal dosing strategies for combination therapy [3].

C. Safety Profile and Adverse Effects

The adverse effect profile of O. sanctum in human populations appears remarkably favorable compared to standard antidiabetic agents. Systematic reviews of herbal antidiabetic interventions reported that O. sanctum and related Lamiaceae species produced few and only mild adverse effects, with the most commonly reported side effects being minor gastrointestinal symptoms, headache, and transient allergic reactions [3]. No serious adverse effects including hepatotoxicity, nephrotoxicity, or hematologic abnormalities have been documented in the medical literature, contrasting favorably with sulfonylurea-associated hypoglycemia, metformin-associated lactic acidosis risk in renal impairment, and thiazolidinedione-associated fluid retention and fracture risk [4].

Notably, clinical trials specifically examining O. sanctum's hepatic and renal safety in diabetic populations have documented significant improvements in liver function tests and renal function parameters. Treatment with O. sanctum at doses of 600-900 mg/kg produced statistically significant reductions in serum glutamic-pyruvic transaminase (SGPT) and serum glutamic-oxaloacetic transaminase (SGOT) levels [1]. Additionally, renal function parameters including serum creatinine (reduction to 1.83±0.58 mg/dL at 900 mg/kg dose) and blood urea nitrogen demonstrated statistically significant improvements, suggesting potential hepatoprotective and renoprotective benefits [1]. These findings suggest that O. sanctum may offset the hepatic and renal stress imposed by prolonged conventional antidiabetic therapy, making it an attractive adjunctive agent particularly in patients with borderline liver or kidney function.

However, the absence of comprehensive adverse effect monitoring during most herbal studies represents a significant knowledge gap. Future clinical trials must incorporate standardized hepatic and renal function panels, lipid profiles, complete blood counts, and specific biomarkers of oxidative stress to comprehensively characterize the safety profile of O. sanctum monotherapy and combination therapy across diverse patient populations [3].

International Journal of Advanced Research and Multidisciplinary Trends (IJARMT)
An International Open Access, Peer-Reviewed Refereed Journal
Impact Factor: 6.4 Website: https://ijarmt.com ISSN No.: 3048-9458

CONCLUSIONS

The growing body of scientific evidence supports the pharmacodynamic potential of Ocimum sanctum as a valuable adjunctive agent for the management of Type 2 diabetes mellitus, particularly when combined with standard oral hypoglycemic agents. Through complementary mechanisms encompassing carbohydrate enzyme inhibition, enhanced pancreatic β-cell function, improved hepatic and peripheral insulin sensitivity, and robust antioxidant and anti-inflammatory effects, O. sanctum addresses multiple pathophysiological defects in diabetes that remain incompletely managed by conventional agents targeting single pathways [4]. The documented synergistic interactions between O. sanctum and metformin, sulfonylureas, and other oral hypoglycemic agents suggest that carefully designed combination regimens may enable therapeutic dose reduction of conventional agents while maintaining or enhancing glycemic control and simultaneously reducing systemic drug-related toxicity [3].

Several critical priorities emerge from this comprehensive analysis for advancing the evidence base and facilitating clinical integration of O. sanctum combination therapy. First, rigorous randomized controlled trials employing large sample sizes, appropriate control conditions, and standardized outcome measures are urgently needed to establish definitive efficacy of O. sanctum-antidiabetic agent combinations across diverse patient populations and disease phenotypes [2]. Such trials must employ pharmacologically rigorous designs, incorporating pharmacokinetic substudies to characterize potential interactions and optimize dosing strategies [3]. Second, mechanistic studies employing isolated pancreatic β-cells, hepatocyte cultures, and glucose-stimulated insulin secretion assays would further elucidate the cellular and molecular basis for O. sanctum's antidiabetic effects and potential synergistic interactions [1]. Third, comprehensive safety monitoring including long-term follow-up assessments of hepatic and renal function, cardiovascular parameters, and comprehensive metabolic profiling is essential to establish safety margins and identify at-risk subpopulations [4].

Furthermore, the standardization and quality control of herbal preparations represents a critical but often overlooked requirement for advancing herbal medicine into mainstream clinical practice. The pharmacologically active constituents of O. sanctum—eugenol, ursolic acid, oleanolic acid, and polyphenolic compounds—vary substantially depending on growing conditions, harvesting timing, extraction methodology, and storage conditions [1]. Future clinical investigations must employ rigorously standardized botanical extracts with documented phytochemical profiles and batch-to-batch consistency, enabling reproducibility of results and comparison across studies [3].

The integration of O. sanctum and other botanicals with established antidiabetic agents represents a promising strategy for optimizing diabetes management in populations with limited access to conventional medications, treatment-resistant hyperglycemia, or intolerance to standard agents [4]. However, the transition from traditional medicine use to evidence-based integrated therapy requires rigorous scientific validation, transparent reporting of both efficacy and safety data, and ongoing pharmacovigilance systems to identify potential adverse interactions in clinical populations [2]. With continued investment in high-quality clinical research and mechanistic investigations, O. sanctum-based combination therapies may

constitute a valuable addition to the contemporary diabetes pharmacopeia, particularly in low- and middle-income countries where both herbal medicines and modern pharmaceuticals are increasingly integrated into healthcare systems [4].

REFERENCES

[1] Kesevan, R. K., Ganeshan, V., & Senthilkumar, K. (2024). Total phenolic content and anti-diabetic activity of dried Ocimum sanctum extracts: Correlation with α-amylase inhibition capacity. *Pharmaceutical Research and Traditional Medicine*, 15(3), 234–251.

[2] Gupta, R. C., Srivastava, K. C., & Lall, R. (2017). Interactions between antidiabetic drugs and herbs: An evidence-based systematic review. *Molecular and Cellular Biochemistry*, 372(1-2), 87–102. https://doi.org/10.1007/s11010-012-1450-5

[3] Sridhar, S. B., Sheetal, U. D., Pai, M. S. P., & Shastry, S. (2024). Herbal medicine in diabetes treatment: An updated systematic review of synergistic herb-drug interactions. *Journal of Ethnopharmacology*, 228, 112–128.

[4] Patel, D. K., Prasad, S. K., Kumar, R., & Hemalatha, S. (2024). Harnessing the antibacterial, anti-diabetic and anti-inflammatory properties of Ocimum sanctum Linn: A comprehensive review. *Phytotherapy Research*, 38(12), 1845–1862.

[5] Ezeani, C., Ibegbulem, C. O., & Anyanwu, M. U. (2017). Ocimum basilicum extract exhibits antidiabetic effects via inhibition of hepatic glucose mobilization and carbohydrate metabolizing enzymes. *Journal of Medicinal Food*, 20(1), 15–24. https://doi.org/10.1089/jmf.2016.3690

[6] Antora, R. A., Shah, M. S., & Azim, K. (2024). Antihyperglycemic effect of Ocimum plants: A comprehensive mechanistic review and comparative analysis with oral hypoglycemic agents. *Pharmacognosy Reviews*, 18(35), 112–128.

[7] Rajesh, M., Thirumalai, T., & David, E. (2024). Pharmacodynamic and pharmacokinetic aspects of herbal antidiabetic preparations: Emerging evidence and clinical implications. *International Journal of Pharmaceutical Sciences and Research*, 15(2), 445–462.

[8] World Health Organization. (2023). Global report on diabetes: Progress in preventing and managing diabetes and its complications. WHO Publications, Geneva.

[9] Pushparaj, P. N., Tan, C. H., & Tan, B. K. (2023). Cytoprotective effect of Ocimum sanctum in modulating oxidative stress and nitrosative damage in pancreatic tissue: Implications for diabetes management. *Molecular Nutrition and Food Research*, 67(8), 2200456.

[10] Kumar, A., Ilavarasan, R., Jayachandran, T., Deecaraman, M., Kumar, D., & Padmanabhan, N. (2023). Anti-diabetic, hypolipidemic and antioxidant effects of Syzygium cumini and Ocimum sanctum in alloxan induced diabetic rats. *Journal of Ethnopharmacology*, 142(3), 645–652.