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An Up-to-Date Review on the Hypoglycemic, Antioxidant, and Hypolipidemic Effects of *Zingiber officinale* in Experimental Diabetes

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Abstract: *Zingiber officinale* Roscoe (ginger), a rhizomatous member of the Zingiberaceae family, has been extensively employed in traditional medicine for the management of metabolic disorders, including diabetes mellitus. Over the past decade, advances in phytochemistry and experimental pharmacology have elucidated a spectrum of bioactive constituents—particularly gingerols, shogaols, paradols, zingerone, and volatile sesquiterpenes—that contribute to its multi-target antidiabetic activity. This review synthesizes up-to 2025 on the hypoglycemic, antioxidant, and hypolipidemic properties of *Z. officinale*, emphasizing data from alloxan- and streptozotocin-induced diabetic models. In diabetic animals, *Z. officinale* improves glycemic control through enhancement of pancreatic β -cell function and insulin secretion, activation of PI3K/Akt and AMPK signaling pathways, suppression of hepatic gluconeogenesis, and modulation of glucose transporters (GLUT2 and GLUT4). Concurrently, ginger attenuates oxidative stress by activating the Nrf2–HO-1 axis, restoring antioxidant enzymes (SOD, CAT, GSH-Px), and reducing lipid peroxidation. In diabetic animals, ginger supplementation consistently improves serum lipid profile ($\downarrow$ TG, $\downarrow$ TC, $\downarrow$ LDL-C, $\uparrow$ HDL-C), decreases hepatic fat accumulation, and mitigates inflammatory responses via NF- κ B inhibition. While preclinical findings strongly support these pleiotropic effects, clinical data remain variable due to differences in extract standardization, dose, and study duration. Standardized preparations rich in [6]-gingerol and [6]-shogaol show the most reproducible metabolic benefits. Collectively, *Z. officinale* represents a mechanistically rich nutraceutical candidate for metabolic support, warranting further well-controlled, standardized trials in diabetic and dyslipidemic populations.

Keywords: *Zingiber officinale*; ginger; streptozotocin; rodents; oxidative stress; hypoglycemic activity.

• Introduction

Diabetes mellitus (DM) represents a major global health burden, affecting an estimated 537 million adults worldwide in 2024. Beyond hyperglycemia, DM is characterized by chronic oxidative stress, dyslipidemia, and low-grade inflammation, leading to micro- and macrovascular complications. Despite available pharmacotherapies—insulin, metformin, and SGLT2 inhibitors—long-term glycemic and oxidative control remain suboptimal, prompting interest in natural multi-target adjuncts.

***Zingiber officinale* Roscoe (ginger)** has been traditionally used in Ayurvedic, Chinese, and Greco-Arab medicine as a digestive and anti-inflammatory tonic. Modern studies highlight its pharmacological versatility, demonstrating antihyperglycemic, antioxidant, hypolipidemic, and insulin-sensitizing actions. Its rhizome contains bioactive constituents—gingerols, shogaols, paradols, diarylheptanoids, and volatile terpenoids (zingiberene, β -bisabolene, curcumene)—that modulate key metabolic pathways, including insulin signaling, hepatic enzyme regulation, redox balance, and lipid oxidation.

• Material and method

For the purpose of conducting this review, the integrated articles were obtained through a systematic search of the Google Scholar database. A total of **100** publications were identified, and after the titles and abstracts were reviewed, **50** papers were selected for full-text reading. According to the inclusion and exclusion criteria, **32** studies were finally considered to summarize the relevant data and to assess the hypoglycemic, antioxidant, and hypolipidemic effects of *Zingiber officinale* in experimental diabetes.

• Results and discussions

Safety Parameter	Experimental / Clinical Findings	Reference Examples	Remarks
Acute toxicity (LD ₅₀)	>5 g·kg ⁻¹ (oral, rodents)	<i>Biomed. Pharmacother.</i> , 2021	Indicates wide safety margin
Sub-chronic toxicity	No mortality or organ pathology at $\leq$ 1 g·kg ⁻¹ /day (90 days)	<i>Life Sci.</i> , 2022	No histopathological alterations
Clinical tolerance	Up to 4 g/day tolerated without serious adverse events	<i>Phytother. Res.</i> , 2023	Mild GI effects in <5% participants
Common adverse effects	Heartburn, mild nausea, flatulence	<i>Front. Nutr.</i> , 2024	Self-limited and reversible
Hepatic & renal safety	Normal ALT, AST, creatinine, urea maintained	<i>J. Ethnopharmacol.</i> , 2023	No hepatotoxicity detected
Reproductive safety	No teratogenic/mutagenic effects ($\leq$ 1 g·kg ⁻¹ /day)	<i>Food Funct.</i> , 2024	Safe for reproductive endpoints

Zingiber officinale has shown consistent antidiabetic potential across alloxan- and streptozotocin-induced models, as well as high-fat-diet experiments. Both aqueous and ethanolic extracts—especially those rich in [6]-gingerol and [6]-shogaol—significantly improved glycemic control, lipid metabolism, and antioxidant status.

Analyzing the selected studies, data on phytochemical composition and bioactive constituents are summarized in **Table 1**, while key molecular mechanisms and experimental outcomes are presented in **Table 2**.

Comparable metabolic responses have been repeatedly observed: decreased fasting glucose and lipid peroxidation (MDA), increased antioxidant enzyme activity (SOD, CAT), and improved lipid profile ($\downarrow$ TG, $\downarrow$ TC, $\uparrow$ HDL-C). In line with these findings, **Al-Amin et al. (2006)** and **Bhandari et al. (2005)** reported significant hypoglycemic and hypolipidemic effects, while **Lee et al. (2015)** demonstrated AMPK-mediated insulin sensitization.

Overall, the evidence supports a **multi-target mechanism**, involving β -cell protection, modulation of insulin signaling, and attenuation of oxidative and inflammatory stress—confirming *Z. officinale* as a promising nutraceutical for metabolic regulation.

• Conclusions

Zingiber officinale is a versatile nutraceutical with well-documented hypoglycemic, antioxidant, and hypolipidemic properties. By modulating insulin secretion, oxidative balance, and lipid metabolism, it offers a multifaceted strategy for managing diabetes mellitus. Its excellent safety profile further supports long-term adjunctive use with standard therapies.

Future research should focus on standardized, gingerol-rich formulations, improved bioavailability (e.g., nanoencapsulation, phytosomal systems), and long-term clinical validation to confirm efficacy and safety. With such advancements, *Z. officinale* may become an evidence-based phytotherapeutic option for metabolic disorders.