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Review Article

Green Tea as Anti-Diabetic: Mechanisms, Epidemiological Evidence, and Clinical Potential

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ABSTRACT

Diabetes mellitus (DM) has reached epidemic proportions globally, necessitating the exploration of safe, cost-effective adjunctive therapies. Green tea (*Camellia sinensis*), particularly epigallocatechin-3-gallate (EGCG) and tea polysaccharides (TPS), has demonstrated significant antidiabetic potential across numerous experimental and clinical settings. This paper provides a comprehensive review of the multifaceted mechanisms through which green tea manages hyperglycemia. These include the potent inhibition of carbohydrate-digesting enzymes alpha-amylase and α-glucosidase, the enhancement of insulin sensitivity, and the protection of pancreatic β-cells from oxidative stress and inflammatory cytokine-induced damage. Some evidence suggests that green tea consumption effectively improves fasting blood glucose (FBG), glycated haemoglobin (HbA1c), and lipid profiles. While bioavailability and clinical inconsistencies remain challenges due to genetic polymorphisms and microbiota variations, green tea is generally considered safe for long-term consumption. In conclusion, green tea stands as a premier bio-functional beverage for the prevention and management of type 2 diabetes and its secondary complications. Future research should prioritize advanced delivery systems, such as nano-encapsulation, to maximise therapeutic outcomes.

Keywords: *Camellia sinensis*; EGCG; GLUT4; Insulin Resistance; *α*-glucosidase; Gut Microbiota; Type 2 Diabetes Mellitus.

Introduction

Chronic hyperglycemia brought on by problems with insulin production, insulin resistance, or both can result in diabetes mellitus (DM), a chronic endocrine illness [1,3]. An estimated 382 million people had metabolic dysfunction in 2013 [2,3,5]. In 90–95% of all cases, type 2 diabetes mellitus (T2DM) is the most common type, which is mostly caused by an increase in obesity and sedentary lifestyles worldwide [3,6]. The main cause of microvascular and macrovascular problems is chronic hyperglycemia linked to diabetes mellitus [7,10].

Green tea has become a powerful bio-functional beverage for the prevention and management of metabolic syndrome and type 2 diabetes [14,16].

In contrast to black or oolong tea, green tea production involves immediate heat treatment to inactivate oxidative enzymes, allowing the leaves to retain high concentrations of bioactive polyphenols, particularly catechins [16,19,20]. The main bioactive components include epigallocatechin-3-gallate (EGCG), which accounts for 50–60% of total catechins, as well as tea polysaccharides (TPS), caffeine, and theanine [3,7,18,19].

Green tea's antihyperglycemic actions are mediated through several specific pathways, according to recent pharmacological studies. These include the strong suppression of small-intestine enzymes that break down carbohydrates, such as α-amylase and α-glucosidase, which delay glucose absorption and reduce post-meal blood sugar increases [20, 21]. Additionally, by encouraging the translocation of glucose transporter 4 (GLUT4) through the activation of PI3K/Akt and AMPK signalling pathways, green tea and its catechins improve insulin sensitivity and glucose uptake in peripheral tissues [7,13].

Additionally, research shows that green tea supports islet regeneration by shielding pancreatic β-cells from oxidative stress and damage caused by inflammatory cytokines [1,2,10].

The search strategy employed keywords such as "Green tea", "EGCG", and "Type 2 Diabetes". Inclusion criteria focused on peer-reviewed RCTs and mechanistic studies, while excluding papers with ambiguous dosage parameters.

Bioactive Composition of Green Tea

The rich and complex chemical profile of green tea (*Camellia sinensis*) is the primary source of its medicinal efficacy [14,18]. In contrast to fermented black tea, green tea is immediately heated to inactivate polyphenol oxidase, which stops catechins from being oxidatively converted into flavones and arubigins [14,16,19]. As a result, green

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tea maintains significant levels of natural polyphenols, which make up about 25–36% of its dry weight [1,5,24].

Polyphenols and Catechins

Polyphenols are the main bioactive components of green tea, with catechins (flavan-3-ols) being the most important subclass [18,21]. (−)-epicatechin (EC), (−)-epigallocatechin (EGC), (−)-epicatechin gallate (ECG), and (−)-epigallocatechin-3-gallate (EGCG) are the four main catechins found in high concentrations [3,7,9]. The most prevalent and biologically active of these is EGCG, which usually makes up 50–60% of the total catechin content [5,7,18]. Along with catechins, green tea also includes phenolic acids, including gallic acid, chlorogenic acid, and caffeic acid, as well as many flavanols like quercetin, kaempferol, and myricetin [3,9,25].

Alkaloids and Amino Acids

The most common purine alkaloid found in green tea is caffeine (methylxanthine), which usually makes up 2% to 5% of the dry weight [5,18]. Theophylline and theobromine are two additional minor alkaloids that contribute to the physiological effects of tea [8,18]. Additionally, 1% to 4% of the dry weight is made up of amino acids, of which L-theanine makes up about 50% [18,24].

Tea Polysaccharides (TPS)

The independent antidiabetic and antioxidant properties of tea polysaccharides (TPS) have attracted a lot of interest lately [3,19]. One or more carbohydrate chains covalently bound to a polypeptide backbone make up TPS [19]. Uronic acid and a variety of monosaccharides, including arabinose and galactose, are abundant in these water-soluble heteropolysaccharides [19,26]. Green tea polysaccharides have been shown to protect pancreatic β-cells and reduce blood glucose through mechanisms involving the cAMP-PKA and PI3K/Akt pathways [19,21].

Essential Minerals and Vitamins

Green tea is an important source of vital minerals and vitamins that improve its bio-functional capability in addition to organic compounds [5,17]. Potassium, phosphorus, calcium, magnesium, and trace elements like zinc, copper, manganese, and fluoride make up about 5% of its dry weight [5,18]. Additionally, vitamins B, C, and E found in green tea work in concert with catechins to counteract reactive oxygen species (ROS) and lessen systemic oxidative stress [18], [1]. Whole green tea extract has more stable pharmacological efficacy than isolated chemicals like pure EGCG, which is frequently attributed to this multi-component synergy [8].

Evidence from Animal Models

The antihyperglycemic effects of green tea are strongly supported by animal models, which enable the investigation of physiological alterations that are challenging to track in human individuals [3,13]. To assess the effectiveness of *Camellia sinensis* extracts, researchers use a variety of models, such as chemical induction (STZ and Alloxan), genetic mutations (db/db and KK-Ay mice), and dietary treatments (High-Fat Diets) [7,16,19].

Streptozotocin (STZ)-Induced Models

By selectively killing pancreatic β-cells through the generation of reactive oxygen species (ROS), streptozotocin is frequently used to cause diabetes [10,27]. Oral administration of green tea extract has repeatedly shown a considerable reduction in fasting blood glucose (FBG) levels in STZ-induced diabetic rats and mice [7,28]. Additionally, drinking green tea successfully reduces glycated haemoglobin (HbA1c) and plasma fructosamine [7,10]. Additionally, research shows that green tea polyphenols enhance the antioxidant profile in STZ-diabetic mice, reducing oxidative stress in organs such as the brain, liver, and kidney [1,10].

Genetic Models: db/db and KK-Ay Mice

A benchmark for researching type 2 diabetes is the db/db mouse model, which displays obesity, hyperinsulinemia, and insulin resistance [23,29]. Green tea catechins have been shown to temporarily reduce mesenteric fat and plasma glucose concentrations in female db/db mice [29]. Green tea considerably reduces glucose intolerance and increases GLUT4 translocation in skeletal muscle in KK-Ay mice, another type 2 model [7].

Alloxan-Induced Models

Another chemical agent that destroys pancreatic islets to cause diabetes is alloxan [8,25]. Crude green tea extract and its aqueous fractions showed strong antihyperglycemic effects and encouraged body weight recovery in studies using alloxan-induced diabetic rabbits [8]. Green tea aqueous extract was shown to have a protective effect against diabetic nephropathy by lowering serum glucose, urea, and creatinine levels in male albino rats [1,25]. According to histological analyses in these models, green tea promotes β-cell regeneration and aids in maintaining the pancreas's structural integrity [1,8].

High-Fat Diet (HFD) and Metabolic Syndrome Models

To simulate human T2DM linked to obesity, models that combine HFD with low-dose STZ are used [2,19]. By lowering total cholesterol (TC), triglycerides (TG), and low-density lipoprotein (LDL) while raising high-density lipoprotein (HDL), green tea polysaccharides (TPS) have demonstrated strong hypoglycemic and anti-obesity effects in these mice [12,19]. Furthermore, ethanol extracts of green tea leaves have been shown to improve insulin secretion and glucose tolerance in HFD-fed rats by inhibiting the DPP-IV enzyme and raising active GLP-1 levels [2].

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3.5 Histopathological and Structural Insights

Green tea reduces vacuolation and steatosis in the liver caused by HFD and STZ [10,19]. Green tea administration cures degenerative changes including necrosis and atrophy in the pancreas and stops islet cells from disappearing [1,27]. Additionally, in db/db mice treated with green tea-based complexes, pancreatic islet size was greatly conserved, supporting its involvement in preserving functional endocrine mass [6].

Epidemiological and Clinical Date

Randomised controlled trials (RCTs) and epidemiological findings provide a multifaceted view of the impact of frequent consumption on metabolic health and diabetes risk [3,15].

Epidemiological Evidence and Population Risk

Green tea has been shown in numerous large-scale population studies to have a preventive effect against type 2 diabetes mellitus (T2DM). Over 40,000 people participated in a historic 10-year follow-up cohort research in Amsterdam, Netherlands, which found that drinking at least three cups of tea (black or green) each day decreased the risk of acquiring type 2 diabetes by about 42% [3]. In a similar vein, research from Japan shows that those who drink six or more cups of green tea per day are 33% less likely to develop diabetes than people who drink less than one cup [15].

Additionally, a study conducted in the UK with an 11.7-year follow-up showed a strong correlation between frequent tea consumption and a lower risk ratio for type 2 diabetes [3]. These results imply that regular, long-term consumption of green tea bioactive substances may considerably reduce the prevalence of metabolic diseases.

Clinical Interventions and Glycemic Control

The immediate and short-term effects of green tea on insulin and glucose dynamics have been the main focus of human clinical research. Green tea intervention significantly improves fasting blood glucose (FBG) and glycated haemoglobin (HbA1c) in T2DM patients, according to a thorough meta-analysis (2024) that included 15 randomised controlled trials and 722 participants [30]. While 14 weeks of green tea consumption significantly enhanced blood antioxidant potential, longer periods may be needed to notice significant changes in HbA1c, according to another clinical investigation in Mauritius with prediabetic and diabetic participants [9]. Additionally, studies on healthy individuals have demonstrated that green tea can enhance glucose metabolism during oral glucose tolerance tests (OGTT), possibly by temporarily reducing plasma glucose levels [28].

Effects on Anthropometric Indices and Blood Pressure

Given that obesity is the main cause of insulin resistance, green tea's ability to help people manage their weight is an essential part of its antidiabetic profile [4]. Diabetic individuals who drank four cups of green tea every day for eight weeks significantly reduced their body weight, body mass index (BMI), and waist circumference in an Iranian randomized clinical trial [4]. Significantly, this study also found that systolic blood pressure significantly decreased, underscoring the cardiovascular advantages of green tea for diabetics [4]. Female populations that follow green tea regimens have shown comparable decreases in waist-to-hip ratios [9].

Impact on Lipid Profiles

Green tea consumption considerably reduces total cholesterol (TC) and low-density lipoprotein (LDL) cholesterol, according to a large meta-analysis of 31 RCTs with 3,321 participants [31]. In studies with extended intervention durations, it was found to lower triglycerides but had no discernible effect on high-density lipoprotein (HDL) [31]. An extra degree of defense against the secondary consequences of diabetes is offered by these lipid-lowering effects [12].

Inconsistencies and Factors Affecting Efficacy

Some clinical trials have found uneven or non-significant results on glycemic management, despite the abundance of good data [15]. Variations in tea processing, the chemical makeup of the extract utilized, dosage, and research duration are frequently blamed for these disparities [3,16]. For example, long-term indicators such as HbA1c may not be affected by short-term dosing (less than 8 weeks) [15]. Furthermore, how different patients react to green tea therapy may depend on individual variations in gut flora, which mediate the metabolism of catechins [22]. Due to genetic variations in the COMT enzyme that affect EGCG metabolism, human clinical outcomes vary. Furthermore, as certain microbial profiles are needed to convert polyphenols into active forms, the composition of the person's gut microbiota is an important mediator [22].

Toxicology

The safety profile of green tea is a vital consideration for its recommendation as a long-term therapeutic adjunctive [5,18]. Green tea is generally recognised as safe (GRAS) when consumed as a beverage at standard dietary levels (up to 8–16 cups per day) [5,17].

No-Observed-Adverse-Effect-Levels (NOAEL)

Green tea extracts are safe even at quite high doses, according to toxicological analyses in mouse models. A NOAEL of around 764 mg/kg/day for males and 820 mg/kg/day for females was determined by chronic 90-day oral toxicity tests in rats [5]. At these doses, neither tissue histopathology nor hematological showed any appreciable toxicological alterations [5].

Hepatotoxicity and Concentrated Extracts

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Standard tea consumption is harmless; however, pure EGCG pills and concentrated green tea extracts (GTE) have drawn criticism [18]. High-dose EGCG consumption, usually above 338 mg/day in sensitive individuals, has been associated with rare incidences of acute liver damage and hepatotoxicity [18]. When catechins are present in too high amounts, oxidative stress and DNA damage are possible mechanisms [18].

Safety in Vulnerable Populations

Research using diabetes animals indicates that green tea may really offer hepatoprotection and nephroprotection by reducing oxidative damage to the kidneys and liver caused by alloxan or STZ [1,25,27]. To improve EGCG stability and bioavailability, future studies should focus on nano-encapsulation. Furthermore, future clinical studies require customized dietary strategies that take baseline gut microbiome and genetic backgrounds into account [31].

Disussion

Green tea has substantial potential as a multi-targeted antidiabetic drug, according to the synthesis of molecular, animal, and clinical evidence [3,11]. Green tea's unusual concentration of gallated catechins, particularly EGCG, which efficiently controls glucose homeostasis through multiple different routes, is the main source of its biological activity [7,18].

Green tea's capacity to concurrently address peripheral insulin resistance and postprandial glucose absorption is one of its main advantages as a functional meal [13,21]. Green tea extract reduces the sharp rise in blood sugar that occurs after consuming carbohydrates [20,21]. Simultaneously, it efficiently addresses the primary pathophysiology of type 2 diabetes mellitus (T2DM) by promoting GLUT4 translocation, which improves glucose elimination in skeletal muscle [6,7].

Nevertheless, there have been significant discrepancies when applying these solid findings from animal models to human populations [3,15]. Some short-term studies (less than 8 weeks) indicate non-significant results, despite the fact that meta-analyses of randomized controlled trials (RCTs) typically confirm significant decreases in fasting blood glucose (FBG) and HbA1c [15,30]. Variations in tea cultivars, processing techniques, and individual variances in catechin bioavailability are probably the causes of these disparities [16,18]. Additionally, the gut microbiota has been identified as a crucial mediator; green tea polyphenols can selectively reduce pathogenic organisms such as Phocaeicola vulgatus, enhancing metabolic results in a donor-dependent way [22].

Conclusion

Green tea is a highly potent bio-functional beverage with significant potential in the prevention and management of diabetes mellitus [3,11,18]. Its antidiabetic efficacy is derived from a multi-targeted pharmacological approach that addresses the fundamental pathologies of type 2 diabetes [7,13]. Green tea effectively mitigates postprandial hyperglycemia by acting as a non-competitive inhibitor of important carbohydrate-digesting enzymes like α-amylase and α-glucosidase [20,21].

Moreover, a strong physiological mechanism for enhancing glucose disposal is provided by its capacity to improve insulin sensitivity by encouraging the translocation of glucose transporter 4 (GLUT4) in skeletal muscle [7,29].

Green tea extract consistently lowers fasting blood glucose, lowers HbA1c levels, and shields pancreatic β-cells from oxidative and inflammatory damage, according to data from specialized animal models [1,8,10].

Human epidemiological data and clinical meta-analyses, which show that frequent use of green tea improves glycemic management, decreases body weight, and lowers systolic blood pressure in diabetic populations, substantially support these findings [4,30,31]. The limited bioavailability of catechins like EGCG and differences in the composition of each person's gut flora are probably the causes of several short-term clinical trials' contradictory results [15,22].

According to toxicological research, green tea has high NOAEL values, indicating that it is safe for long-term dietary consumption [5,18]. To prevent possible hepatotoxicity, however, high concentrations of EGCG supplements should be used with caution [18].

To sum up, green tea is a safe, economical, and scientifically proven supplemental treatment. A promising non-pharmacological approach to reducing the worldwide burden of diabetes mellitus and its related cardiovascular and renal consequences is incorporating green tea into daily dietary regimens [11,17].

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