Epigallocatechin Gallate (EGCG) and Chlorogenic Acid (CGA) as Anti-Vascular Calcification Agents in Diabetes Mellitus: A Literature Review

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Abstract. The abstract should summarize the contents of the paper in short terms, i.e. 15–250 Vascular calcification is a major complication of diabetes mellitus, driven by hyperglycemia, oxidative stress, inflammation, and advanced glycation end products (AGEs), which collectively promote osteogenic transdifferentiation of vascular smooth muscle cells (VSMCs). Despite its clinical significance, no approved pharmacotherapy directly prevents or reverses this process. Epigallocatechin-3-gallate (EGCG) and chlorogenic acid (CGA), polyphenolic compounds derived from green tea and coffee, respectively, have emerged as promising nutraceutical candidates due to their antioxidant, anti-inflammatory, and metabolic properties. This literature review synthesizes evidence from in vitro, in vivo, and clinical/translational studies examining the anti-vascular calcification potential of EGCG and CGA in the context of diabetes mellitus. EGCG inhibits VSMC osteogenic differentiation by suppressing the JunB transcription factor and MAPK/ERK signaling, reducing calcium deposition and osteogenic markers (Runx2, ALP) while preserving a contractile VSMC phenotype. In vivo, EGCG attenuated aortic calcification and improved glycemic and lipid profiles in diabetic animal models, and a clinical randomized controlled trial confirmed its cardiovascular benefits in type 2 diabetes mellitus patients. CGA exerts anti-calcification effects by inhibiting AGE formation via carbonyl trapping and attenuating endothelial calcium overload and oxidative stress through TRPC channel inhibition, with in vivo evidence showing synergistic activity with EGCG in reducing aortic osteogenic markers. Together, EGCG and CGA target complementary pathogenic pathways of diabetic vascular calcification, suggesting their potential as adjunctive therapeutic agents. Further dedicated clinical trials are warranted to establish their efficacy and safety in preventing arterial calcification in diabetic populations.

Keywords: Epigallocatechin-3-gallate (EGCG), Chlorogenic acid (CGA), Vascular calcification, Diabetes mellitus, Osteogenic differentiation.

1 Introduction

Vascular calcification is a pathological deposition of calcium-phosphate (hydroxyapatite) in the vessel wall that leads to arterial stiffening and elevated cardiovascular risk [1,2]. Diabetes mellitus markedly accelerates vascular calcification, as chronic hyperglycemia and dyslipidemia promote osteogenic transformation of

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vascular smooth muscle cells (VSMCs) through oxidative stress, inflammation, and advanced glycation end products (AGEs) [2]. Indeed, diabetic patients show earlier and more extensive arterial calcification than non-diabetics, and calcified arteries in diabetes often exhibit VSMCs with bone-like (osteochondrogenic) phenotypes [2]. Currently, there are no approved pharmacotherapies that directly prevent or reverse vascular calcification. This has spurred interest in nutraceutical or adjunctive therapies that target the mechanisms of calcification.

Epigallocatechin-3-gallate (EGCG) and chlorogenic acid (CGA) are polyphenolic compounds abundant in green tea and coffee, respectively, known for antioxidant and anti-inflammatory properties. Both have demonstrated beneficial effects on cardiovascular and metabolic health, including improved endothelial function and glycemic control [3,4]. In the context of diabetes, EGCG and CGA may counteract the pathways driving vascular calcification. This review examines in vitro, in vivo, and clinical/translational studies on EGCG and CGA as inhibitors of vascular calcification under diabetic conditions, highlighting their mechanisms of action (e.g. effects on osteogenic signaling in VSMCs, AGE-RAGE pathways, oxidative stress, and inflammation) and the evidence of efficacy.

2 Materials and Methods

This narrative literature review was conducted by analyzing published studies evaluating the roles of Epigallocatechin-3-gallate (EGCG) and Chlorogenic Acid (CGA) in the pathophysiology of diabetes mellitus and its associated complications. The selected literature encompassed a variety of study designs to provide a comprehensive mechanistic understanding, ranging from molecular-level investigations to clinical manifestations. The search strategy focused on identifying relevant studies using the following keywords: "epigallocatechin-3-gallate," "chlorogenic acid," "oxidative stress," "endothelial dysfunction," and "diabetic retinopathy." Literature searches were performed across major scientific databases including PubMed, Scopus, and Google Scholar, without restriction on publication year, to ensure broad coverage of available evidence.

The materials analyzed included randomized double-blind placebo-controlled trials involving patients with type 2 diabetes mellitus (T2DM), which were used to evaluate the interaction between genetic polymorphisms and antioxidant supplementation. Inclusion criteria for clinical studies required a confirmed diagnosis of T2DM, administration of EGCG or CGA supplementation, and the reporting of at least one outcome relevant to metabolic parameters, oxidative stress markers, or vascular function. Studies were excluded if they lacked a control group or reported insufficient methodological detail.

In addition, this review synthesized data from in vivo experimental studies utilizing male rodent models — including Sprague-Dawley and Wistar rat strains — in which diabetes was induced either by streptozotocin (STZ) injection or a high-sucrose high-fat diet. These studies were selected to assess the effects of EGCG and CGA on metabolic parameters (e.g., fasting blood glucose, lipid profiles), oxidative stress

biomarkers (e.g., malondialdehyde, superoxide dismutase), and enzymatic activity relevant to vascular calcification.

To further elucidate cellular mechanisms, this review also incorporated in vitro studies employing cell culture models, including human retinal endothelial cells (HRECs) and microglial cells, to investigate EGCG- and CGA-mediated angiogenic and inflammatory signaling pathways. Furthermore, a pharmaceutical technology perspective was included through the analysis of studies comparing the efficacy of standard EGCG solution with nano-liposomal formulations in modulating matrix metalloproteinase (MMP) activity, providing insights into bioavailability and targeted drug delivery considerations.

Data from all included sources were narratively synthesized to explore the therapeutic potential of EGCG and CGA in preventing vascular complications associated with diabetes mellitus. Due to the heterogeneity of study designs, populations, and outcome measures, a formal meta-analysis was not performed. Instead, findings were organized thematically according to study type (in vitro, in vivo, and clinical) and mechanism of action to allow for a structured and comprehensive evaluation of the evidence.

3 Results

3.1 Result of Epigallocatechin Gallate (EGCG)

In Vitro Studies. Multiple in vitro studies demonstrate EGCG's ability to directly inhibit the calcific transformation of vascular cells. In cultured human aortic smooth muscle cells (HASMCs) under high-phosphate calcifying conditions, EGCG significantly reduced calcium deposition and alkaline phosphatase (ALP) activity in a dose-dependent manner [5]. EGCG treatment (at micromolar concentrations) not only decreased mineralization, but also favorably modulated the phenotype of vascular smooth muscle cells (VSMCs). Specifically, EGCG suppressed osteogenic markers such as runt-related transcription factor 2 (Runx2), ALP, and matrix metalloproteinases (MMP2/9), while upregulating contractile markers (e.g. α-smooth muscle actin and SM22α) that are normally lost during osteogenic differentiation [5,6]. These findings indicate that EGCG directly inhibits the osteogenic differentiation of VSMCs under pro-calcification stress in vitro [5,6].

Mechanistically, this effect involves down-regulation of the JunB transcription factor – a regulator found to be abnormally activated in calcifying VSMCs. EGCG exposure prevented the increase in JunB expression induced by a calcifying medium, and subsequent analyses confirmed that silencing JunB enhanced EGCG's anti-calcification effect, whereas overexpression of JunB attenuated it [5,6]. In parallel, EGCG was shown to modulate the extracellular signal–regulated kinase pathway, as co-treatment with the MEK/ERK inhibitor PD98059 mirrored EGCG's suppression of osteogenic signaling [5,6]. Collectively, the in vitro evidence establishes that EGCG can block the molecular cascade of vascular calcification, preserving a VSMC contractile phenotype and preventing pathological calcium accumulation [5,6].

EGCG has been shown to directly counteract high-glucose-induced cellular dysfunction in vitro. A review reported that EGCG treatment inhibits the aberrant proliferation of vascular smooth muscle cells (VSMCs) under high glucose conditions and suppresses high glucose-mediated inflammatory activation of endothelial cells [7]. These findings suggest that EGCG can mitigate early pro-calcific changes at the cellular level, such as VSMC growth and vascular inflammation, which are precipitated by diabetic hyperglycemia.

In Vivo Studies. Animal model studies provide further support for EGCG's anti-calcification role in diabetic contexts. In a mouse model of medial arterial calcification (MAC) – induced by high-dose vitamin D3 to mimic calcification as seen in diabetes – oral EGCG administration for 8 weeks markedly reduced aortic calcium deposition compared to untreated controls [5]. Treated mice showed visibly less Alizarin Red-positive calcific area in the aorta, indicating an inhibition of vascular mineralization [5] . Histological analysis revealed that EGCG preserved the integrity of vascular structure: EGCG-treated calcified aortas maintained continuous, wavy elastic fibers, whereas untreated calcified vessels exhibited disrupted architecture [5]. Consistent with the in vitro results, EGCG in vivo reversed osteogenic protein expression changes in calcified arteries – increasing VSMC contractile proteins and decreasing bone-like markers that had been elevated by the calcifying stimulus [5]. Another study examined EGCG's effects in a chronic kidney disease-associated calcification model, which shares pathogenic features with diabetes-related vascular calcification. There, EGCG supplementation similarly inhibited osteogenic transformation of VSMCs in the arterial wall via targeted inactivation of JunB, ultimately protecting against medial calcification [5]. This highlights JunB as a common molecular target of EGCG in suppressing vascular calcification across different disease settings.

Importantly, EGCG's benefits extend to metabolic syndrome and diabetic models, which closely relate to type 2 diabetes. Study reported that in high-fat/high-sugar diet rats (a metabolic syndrome model), green tea extract (rich in EGCG) given for 9 weeks significantly attenuated early aortic calcification [8]. The treated rats had lower aortic Runx2 and osteopontin levels – markers of osteogenic activity – compared to untreated controls, indicating reduced calcification signaling [8]. Notably, the combination of green tea (EGCG source) and green coffee (CGA source) extracts was more effective at lowering these calcification markers than the anti-diabetic drug metformin alone [8]. The intervention also enhanced protective signaling in the vasculature: AKT1 and mTOR expression in the aorta were increased in the extract-treated group, suggesting activation of pro-survival/anti-calcification pathways, while osteogenic drivers were dampened [8]. These findings in a metabolic syndrome context imply that EGCG can impede diabetes-related vascular calcification, likely by improving the metabolic milieu and directly modulating calcification regulators in the vessel wall.

EGCG's ability to improve the diabetic metabolic environment may itself contribute to reducing calcification risk. In streptozotocin-induced diabetic rats, a lipophilic EGCG derivative significantly lowered chronic hyperglycemia (reducing blood glucose by ~40%) and improved the lipid profile over 30 days [9]. This

compound acted as an α-glucosidase inhibitor, slowing carbohydrate absorption and postprandial glucose spikes [9]. Consistently, an in silico molecular docking study confirmed that EGCG binds to and can inhibit the α-glucosidase enzyme, supporting a mechanism for its glycemic control effects [10]. By mitigating hyperglycemia and dyslipidemia – key drivers of vascular damage – EGCG and its derivatives address upstream factors that promote calcific complications in diabetes.

Clinical Research. Clinical evidence for EGCG's impact on vascular calcification in diabetes is still emerging. A double-blind randomized controlled trial investigated EGCG supplementation in patients with type 2 diabetes mellitus [11]. In this study, 60 T2DM patients received 300 mg/day of EGCG or placebo for 2 months, and outcomes related to cardiovascular risk and inflammation were measured. EGCG treatment resulted in significant reductions in body mass index (BMI), diastolic blood pressure, mean arterial pressure, and total cholesterol levels in a subset of patients carrying a common risk allele of the FTO gene [11]. In general, EGCG tended to improve lipid profiles and blood pressure without adverse effects. Inflammatory biomarkers such as IL-6 and C-reactive protein showed a decreasing trend with EGCG, although the magnitude of change depended on the patient's genotype [11]. While this trial did not directly measure vascular calcification, the improvements in blood pressure, cholesterol, and inflammatory status are indicative of a reduced pro-calcific burden in the vascular system. Moreover, the differential response based on FTO genotype suggests patient-specific factors may influence EGCG's efficacy in a clinical setting [11]. Overall, this pilot clinical study supports the safety and metabolic benefits of EGCG in diabetic patients, providing a rationale for further trials focusing on hard outcomes such as arterial calcification and cardiovascular events.

3.2 Result of Chlorogenic Acid (CGA)

In Vitro Studies. CGA has shown protective effects on vascular cells under diabetic and pro-calcific conditions in several in vitro experiments. One key mechanism by which diabetes drives vascular calcification is through the formation of advanced glycation end-products (AGEs), which stiffen vessels and induce osteogenic signaling. A study demonstrated that CGA can directly inhibit AGE formation in a high-glucose environment [12]. In an in vitro glycation assay, CGA dose-dependently suppressed the generation of AGEs from bovine serum albumin and glucose, with an IC_{50} of ~148 Mm [12].This anti-glycation potency was superior to that of aminoguanidine, a known pharmaceutical AGE inhibitor [12]. Furthermore, CGA prevented the cross-linking of AGE-modified proteins to collagen, a process that contributes to vascular stiffness and calcific matrix deposition [12]. The study suggested that CGA likely traps reactive carbonyl intermediates (such as methylglyoxal), thereby impeding the Maillard reactions that lead to AGEs [12]. By reducing AGE accumulation and protein cross-links, CGA may help preserve vascular elasticity and prevent calcification in diabetic tissues, since AGEs are implicated in calcific atherosclerosis and arterial media sclerosis.

CGA has also been shown to protect endothelial cells from pro-atherogenic calcium stress, which is relevant to early calcific changes. A study treated human endothelial cells with lysophosphatidylcholine (LPC), a component of oxidized LDL that raises intracellular calcium and ROS, mimicking diabetes-associated oxidative damage [13]. They found that CGA markedly attenuated LPC-induced Ca^{2+} influx in endothelial cells by inhibiting store-operated calcium entry through Transient Receptor Potential Canonical (TRPC) channels [13]. CGA exposure prevented the pathological rise in cytosolic [Ca^{2+}] that triggers inflammation and cell death, and it concomitantly reduced reactive oxygen species generation in the cells [13]. As a result, CGA protected endothelial cell viability from LPC toxicity, indicating less endothelial injury [13]. Given that endothelial dysfunction and inflammation precede and promote vascular calcification in diabetes, CGA's ability to stabilize calcium homeostasis and oxidative stress in endothelium has significant implications. These in vitro findings suggest CGA can interrupt early mechanisms of diabetic vascular injury – such as AGE formation and calcium overload – which collectively contribute to calcification. By preventing biochemical triggers of calcification (glycation, oxidative Ca^{2+} signaling), CGA demonstrates a potent anti-calcification capacity at the cellular level.

In Vivo Studies. Direct in vivo evidence for CGA's anti-vascular calcification effect in diabetes comes primarily from studies of diets or extracts rich in this polyphenol. As part of the metabolic syndrome rat experiment mentioned earlier, green coffee extract (a rich source of CGA) was combined with green tea extract to evaluate prevention of vascular calcification. In those rats, the addition of green coffee (200 mg/kg) significantly enhanced the anti-calcification outcome: animals receiving both green coffee (CGA) and green tea (EGCG) showed the greatest reduction in aortic osteogenic markers and vascular inflammation, compared to untreated metabolic syndrome rats [8]. The group given the CGA-containing extract had lower serum osteopontin (an inflammatory bone matrix protein) and reduced aortic Runx2 expression, indicating that CGA contributed to blunting the calcification signaling cascade in vivo [8] .These improvements were accompanied by better metabolic profiles (lower fasting glucose and triglycerides) and blood pressure in the treated rats [8], consistent with CGA's known hypoglycemic and antioxidant effects. Although CGA alone was not isolated in this model, the results imply that CGA synergizes with EGCG to confer cardiovascular protection, partly by activating AKT1 and related pathways that oppose vascular calcification [8].

Beyond calcification-specific outcomes, other animal studies reinforce CGA's beneficial actions on diabetic vasculature. Dietary CGA has been associated with improved endothelial function and reduced oxidative stress in diabetic conditions [13]. Its ability to inhibit glycoxidation may translate into less arterial stiffening and calcific deposition over time [12]. However, dedicated in vivo studies focusing on CGA's impact on vascular calcium accumulation in diabetic models are still limited. The provided research suggests that CGA addresses several pathogenic processes (hyperglycemia, AGE formation, endothelial dysfunction) that collectively underlie vascular calcification in diabetes. Thus, while in vivo evidence is relatively sparse compared to EGCG, the mechanistic data indicate that CGA can attenuate the

development of calcification in the diabetic vasculature by improving metabolic and molecular risk factors.

Clinical Research. To date, clinical evidence specifically evaluating the effects of chlorogenic acid (CGA) on vascular calcification in individuals with diabetes mellitus remains limited. None of the currently available studies, including those reviewed herein, report clinical trials directly assessing CGA's efficacy in preventing or attenuating arterial calcification in this population.

Initial clinical studies, though not yet focused on calcification endpoints, suggest that CGA confers cardiovascular benefits in humans. For instance, hypertensive patients consuming CGA-enriched green coffee extract showed modest but significant reductions in systolic and diastolic blood pressure over 4–12 weeks. Additionally, a placebo-controlled trial reported that a single high-CGA coffee dose improved postprandial flow-mediated dilation (FMD) and reduced oxidative stress markers, ameliorating endothelial dysfunction in subjects with borderline hypertension. These findings indicate that CGA can improve vascular function and reduce risk factors in humans, supporting its potential translation as a therapy to mitigate vascular injury (including calcification) in diabetic populations [4].

4 Conclusion

This literature review demonstrates that both epigallocatechin-3-gallate (EGCG) and chlorogenic acid (CGA) hold considerable promise as adjunctive agents against vascular calcification in the context of diabetes mellitus. The available evidence, spanning in vitro, in vivo, and early clinical studies, reveals that these two polyphenols act through distinct yet complementary mechanisms to counteract the major pathogenic drivers of diabetic vascular calcification.

EGCG exerts its anti-calcification effects primarily by suppressing the osteogenic transdifferentiation of vascular smooth muscle cells (VSMCs). Through downregulation of the JunB transcription factor and inhibition of the MAPK/ERK signaling pathway, EGCG reduces the expression of osteogenic markers such as Runx2 and ALP while preserving the contractile VSMC phenotype. These molecular effects have been validated across multiple in vivo models of vascular calcification, including vitamin D_3-induced medial arterial calcification and chronic kidney disease models, where EGCG consistently attenuated aortic calcium deposition and maintained vascular structural integrity. Moreover, EGCG and its lipophilic derivatives improve the diabetic metabolic environment by lowering hyperglycemia and dyslipidemia via α-glucosidase inhibition, thereby addressing upstream risk factors that drive calcific progression. A clinical randomized controlled trial further supports its safety and cardiovascular benefits in type 2 diabetes mellitus patients, although direct measurement of calcification endpoints in clinical settings is still lacking.

CGA, in turn, targets earlier and distinct stages of the calcification cascade. Its capacity to inhibit advanced glycation end-product (AGE) formation through carbonyl-

trapping mechanisms directly counters one of the most potent diabetes-specific drivers of vascular stiffening and calcification. Additionally, CGA protects vascular endothelium by attenuating oxidative calcium influx via TRPC channel inhibition, thereby reducing endothelial dysfunction — a key precursor to calcific vascular disease. In vivo, CGA demonstrated synergistic activity with EGCG in a metabolic syndrome model, producing greater reductions in aortic osteogenic markers than either compound alone. Clinical evidence for CGA, while not yet focused on calcification endpoints, suggests beneficial effects on blood pressure and endothelial function in humans.

Despite these encouraging findings, several important limitations must be acknowledged. Most in vivo studies were conducted in non-diabetic calcification models (e.g., vitamin D_3-induced or CKD-associated), limiting direct extrapolation to the diabetic context. Clinical evidence remains scarce, with no trials to date directly measuring the impact of EGCG or CGA on arterial calcification scores in diabetic patients. Additionally, questions around optimal dosing, bioavailability, long-term safety, and potential drug interactions have not been fully resolved.

In conclusion, EGCG and CGA represent mechanistically well-grounded, naturally derived candidates for the prevention or attenuation of vascular calcification in diabetes mellitus. Their complementary actions on VSMC osteogenesis, AGE formation, oxidative stress, and endothelial dysfunction collectively address the multifactorial nature of diabetic vascular disease. Future research should prioritize well-designed clinical trials in diabetic populations using validated calcification imaging endpoints, as well as pharmacokinetic studies to optimize the therapeutic application of these polyphenolic compounds.

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Table 1. Extracted Data from Studies

Author, Year	Compound (Study)	Model / Study Type	Key Findings	Mechanisms Identified	Relevance to Diabetes-Related Vascular Calcification
Li et al., 2025	EGCG	In vivo (CKD-induced medial arterial calcification rat model); in vitro (osteogenic VSMCs)	EGCG significantly reduced calcium deposition and osteogenic differentiation of vascular smooth muscle cells (VSMCs) in CKD-induced medial arterial calcification.	Suppression of JunB transcription factor activity via inhibition of the Ras/Raf/MEK/ERK signaling pathway, leading to reduced VSMC osteogenic transdifferentiation.	**Indirect relevance:** Study used a CKD model rather than diabetes. However, inhibition of VSMC osteogenic transition is a core mechanism in diabetes-related vascular calcification.
Li et al., 2025	EGCG	In vivo (vitamin D_3–induced aortic calcification in rats); in vitro (human aortic smooth muscle cells under high phosphate)	EGCG dose-dependently reduced aortic calcium deposition in vivo and inhibited phosphate-induced calcification in HASMCs in vitro.	Downregulation of AP-1 component JunB and suppression of MAPK/ERK signaling, preventing osteogenic phenotype switching in VSMCs.	**Indirect relevance:** Not a diabetic model, but directly targets molecular pathways (JunB, Runx2) known to drive vascular calcification in diabetes.
Rohman et	EGCG	In vivo (metabolic	Combination therapy	Activation of AKT/mTOR	**Indirect relevance:** Model represents

Author, Year	Compound (Study)	Model / Study Type	Key Findings	Mechanisms Identified	Relevance to Diabetes-Related Vascular Calcification
al., 2024		syndrome rat model; green tea + green coffee extract)	significantly increased AKT1 and mTOR expression while reducing RUNX2 and osteopontin expression in aortic tissue, indicating inhibition of vascular calcification processes.	signaling and suppression of osteogenic transcription markers in vascular tissue.	metabolic syndrome (pre-diabetic state). Findings are mechanistically relevant to diabetes-associated vascular calcification.
Rohman et al., 2024	CGA	In vivo (metabolic syndrome rat model; green coffee + green tea extract)	Green coffee extract (CGA-containing) contributed to reduced osteogenic marker expression and improved vascular signaling when combined with EGCG.	Enhancement of AKT1/mTOR signaling and suppression of RUNX2/OPN-mediated osteogenesis.	**Indirect relevance:** Not a diabetic model, but metabolic syndrome shares pathophysiological drivers of diabetic vascular calcification.
Jung et al., 2017	CGA	In vitro (HUVECs exposed to lysophosphatidylcho	CGA protected endothelial cells from LPC-	Inhibition of TRPC1-mediated Ca^{2+} entry and suppression of	**Indirect relevance:** Endothelial dysfunction precedes vascular calcification in diabetes; CGA

Author, Year	Compound (Study)	Model / Study Type	Key Findings	Mechanisms Identified	Relevance to Diabetes-Related Vascular Calcification
		line / ox-LDL)	induced injury by reducing intracellular Ca^{2+} influx and ROS production, restoring cell viability.	oxidative stress pathways.	mitigates upstream oxidative and inflammatory triggers.
Kim et al., 2011	CGA	In vitro (AGE formation assays with BSA–glucose system)	CGA strongly inhibited advanced glycation end-product (AGE) formation and AGE–collagen crosslinking, more effectively than aminoguanidine.	Trapping of reactive carbonyl intermediates (e.g., methylglyoxal), reducing AGE accumulation.	**Indirect relevance:** AGE accumulation is a major driver of vascular stiffness and calcification in diabetes.
Li et al., 2007	EGCG (lipophilic derivative)	In vivo (STZ-induced diabetic rats); in vitro (α-glucosidase inhibition)	EGCG derivative significantly reduced fasting glucose, improved glucose tolerance, and lowered TG, TC, and LDL in diabetic rats.	Inhibition of intestinal α-glucosidase leading to reduced postprandial hyperglycemia.	**Indirect relevance:** Improved glycemic and lipid control reduces metabolic drivers of vascular calcification in diabetes.

Author, Year	Compound (Study)	Model / Study Type	Key Findings	Mechanisms Identified	Relevance to Diabetes-Related Vascular Calcification
Hosseini et al., 2021	EGCG	Clinical trial (double-blind RCT; 60 T2DM patients, 8 weeks)	EGCG supplementation reduced BMI, diastolic blood pressure, mean arterial pressure, and total cholesterol, particularly in FTO risk allele carriers.	Likely mediated by antioxidant and anti-inflammatory effects; gene–nutrient interaction with FTO polymorphism.	**Indirect relevance:** Improvement of cardiovascular risk factors in diabetes may attenuate progression of vascular calcification.
Yohana et al., 2024	EGCG	In silico (molecular docking to α-glucosidase)	EGCG showed stable binding to α-glucosidase with favorable affinity and non-toxic predicted profile, though with Lipinski violations.	Direct interaction with α-glucosidase active-site residues via hydrogen and hydrophobic bonds.	**Indirect relevance:** Supports glucose-lowering potential, indirectly reducing hyperglycemia-driven vascular calcification risk.

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