Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/2m3r1196

# TARGETING INFLAMMATION IN ATHEROSCLEROSIS: INSIGHTS FROM NATURAL AND CONVENTIONAL THERAPIES

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**Abstract**

Atherosclerosis, a cardiovascular disease is known to be one of the major causes of mortality across the globe. It has been predicted that within few years atherosclerosis will be responsible for much greater number of worldwide mortalities. Cardiovascular disease accounts for primary number of all deaths in North America and European countries [1]. Atherosclerosis is derived from the Greek words 'athero' meaning paste and 'sclerosis' which means hardening. Atherosclerosis is a multifactorial disease characterized by immune-inflammatory processes and lipid deposition in arterial walls, leading to plaque formation and progressive narrowing of blood vessels [2]. This pathology is a major cause of coronary artery disease, myocardial infarction, and stroke. While elevated low-density lipoprotein cholesterol (LDL-C), hypertension, and smoking are established risk factors, emerging contributors such as poor sleep, sedentary lifestyle, microbiome imbalance, environmental pollutants, and psychological stress are increasingly recognized. Together, these factors accelerate plaque growth, vascular dysfunction, and thrombus formation, culminating in severe cardiovascular events.

Therapeutic approaches for atherosclerosis target both lipid accumulation and inflammation. Natural compounds like Secoisolariciresinol Diglucoside (SDG), flaxseed lignans, flavonoids (quercetin, anthocyanins), and the medicinal plant *Sphaeranthus indicus* demonstrate lipid-lowering, antioxidant, and anti-inflammatory effects. Canakinumab, an anti-inflammatory biologic, and Ninjurin1 (NINJ1), a novel immune modulator, show promise as emerging targets. Alongside these, conventional drugs such as nifedipine, ramipril, and perindopril remain critical in managing blood pressure and reducing cardiovascular risk.

This review emphasizes the interplay of traditional and non-traditional risk factors in atherosclerosis while outlining both established and innovative therapeutic strategies aimed at reducing disease burden and improving cardiovascular outcomes.

**Keywords:** Inflammation, Atherosclerosis, Natural Products, Clinical trials

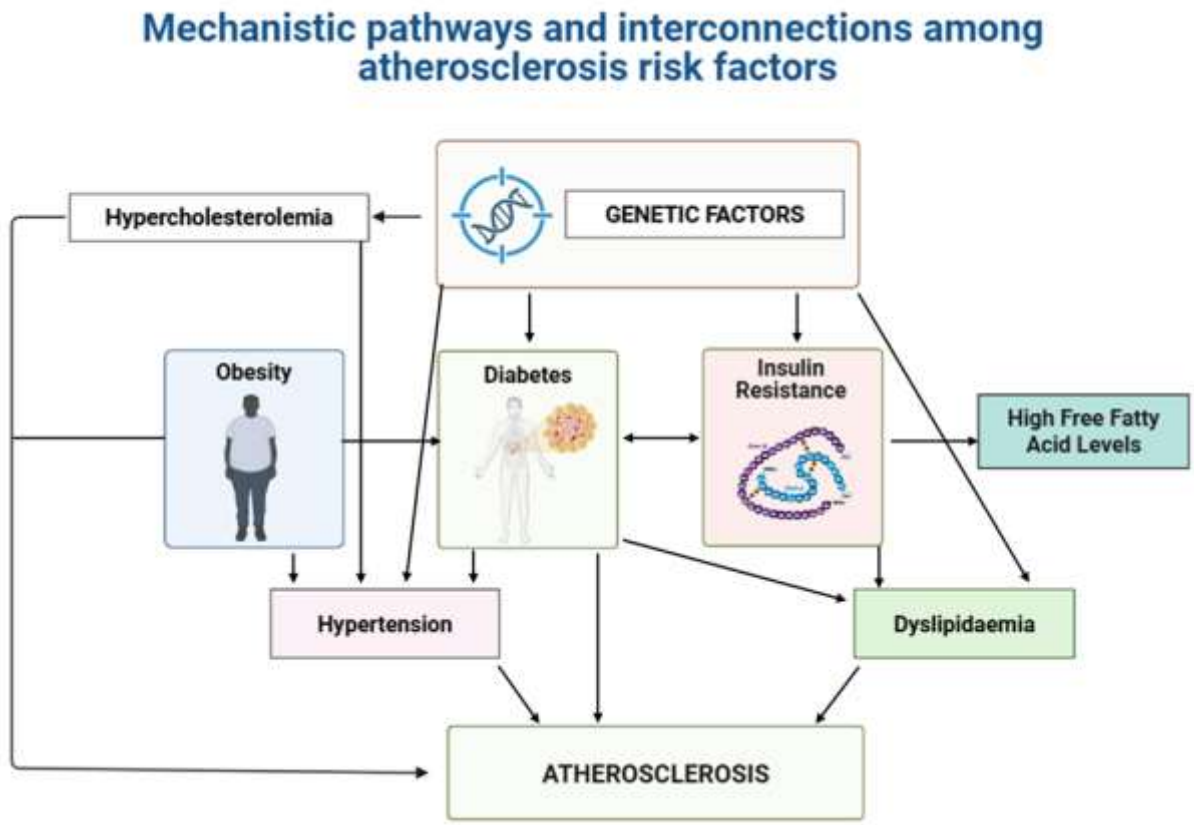


**Figure 1:** Mechanistic pathways and interconnections among atherosclerosis risk factors

## 1. Inflammation and initiation of Atherosclerosis

Inflammation is a central driver of atherosclerosis, beginning with endothelial activation that promotes monocyte recruitment, their differentiation into macrophages and foam cells, and the release of pro-inflammatory cytokines. Pyroptosis, a caspase-dependent form of programmed cell death mediated by gasdermin D, further amplifies this response by inducing cell lysis and cytokine release. While initially described as an antimicrobial defense, pyroptosis is increasingly recognized in chronic inflammatory disorders and is now linked to vascular pathology, including early atherogenesis [2].

Alongside immune cells, vascular smooth muscle cells (SMCs) contribute significantly to plaque initiation. By altering extracellular matrix composition, facilitating lipid retention, and adopting foam cell–like phenotypes, SMCs participate directly in lesion development. They also express adhesion molecules that enhance leukocyte recruitment and produce cytokines such as PDGF, TGF-β, IFNγ, and MCP-1, thereby amplifying local inflammation. Although traditionally associated with fibrous cap formation in advanced lesions, recent gene-targeting studies underscore their pivotal role in the earliest phases of plaque progression [3].

Toll-like receptor 4 (TLR4) further integrates inflammatory signalling into atherogenesis. Beyond recognizing microbial ligands, TLR4 responds to endogenous molecules released during vascular injury, thereby sustaining chronic inflammation. Evidence from TLR4-deficient mouse models and human polymorphism studies highlights its importance in both the initiation and progression of atherosclerotic disease [4].

## 2. Disease Progression in Atherosclerosis

The initiation of atherosclerosis is closely linked to dysregulation of lipid metabolism. Under normal conditions, LDL receptor expression is downregulated once intracellular cholesterol requirements are met. However, excessive lipid intake, defective receptor function, or genetic mutations disrupt this control, leading to intimal retention of LDL particles [5,6]. These lipoproteins bind to arterial proteoglycans, becoming prone to oxidative and enzymatic modification, a hallmark of early lesion development [7,8]. Oxidized LDL (oxLDL), generated through vascular NADPH oxidases,

lipoxygenases, or myeloperoxidase activity, promotes endothelial dysfunction by enhancing permeability, leukocyte adhesion, and pro-coagulant activity [7,9]. Endothelial cells upregulate adhesion molecules such as VCAM-1, ICAM-1, and P-selectins, facilitating monocyte recruitment. MCP-1, secreted by endothelial and smooth muscle cells, further drives monocyte migration into the intima. Genetic studies in mice deficient in VCAM-1 or MCP-1 confirm their critical role in early lesion formation [8, 10]. Activated T cells entering via VCAM-1 amplify inflammation through cytokines including IFN-γ and TNF-β, which stimulate macrophages, endothelium, and smooth muscle cells [10].

Once within the intima, monocytes differentiate into macrophages under the influence of macrophage colony-stimulating factor (M-CSF), which upregulates scavenger receptor-A expression and drives uptake of modified LDL to form foam cells [11-13]. Foam cell accumulation creates the fatty streak, the earliest visible atherosclerotic lesion. The local environment is enriched with pro-inflammatory mediators such as cytokines, chemokines, eicosanoids, and platelet-activating factor, sustaining chronic inflammation [7,10,12]. Excessive reactive oxygen species (ROS) production overwhelms antioxidant defenses, exacerbating oxidative stress and arterial injury [7,10,14]. Activated macrophages and lymphocytes release hydrolytic enzymes, growth factors, and inflammatory mediators, perpetuating lesion expansion [8-10]. Importantly, uptake of oxLDL, apoptotic debris, and microbial products through scavenger and Toll-like receptors further activates macrophages. Supporting this, studies in apoE- and TLR-deficient mice revealed reduced lesion formation, highlighting the importance of innate immune signalling in foam cell development [15].

Progression from fatty streaks to advanced atherosclerotic lesions involves migration and proliferation of smooth muscle cells (SMCs) into the intima, accompanied by extracellular matrix (ECM) accumulation and arterial wall remodelling. This remodelling may include compensatory enlargement or calcification, contributing to plaque hardening [5,7]. Activated leukocytes and vascular cells secrete fibrogenic mediators and growth factors, promoting SMC proliferation and synthesis of a dense ECM, which forms the fibrous cap. Platelet-derived growth factor (PDGF), secreted by activated macrophages, is a key driver of SMC migration and proliferation and is consistently overexpressed in human lesions. However, T cell–mediated SMC apoptosis destabilizes plaque structure, further complicating disease progression [8].

In advanced disease, plaque stability declines as activated macrophages secrete proteolytic enzymes, including matrix metalloproteinases (MMPs), which degrade collagen and other ECM components of the fibrous cap [10,15]. Interactions between CD40/CD40L on T cells and macrophages amplify inflammatory signalling, leading to production of tissue factor (TF), MMPs, and pro-inflammatory cytokines [16]. OxLDL, ROS, TNF-α, and IL-1 further enhance MMP expression by foam cells and SMCs, weakening plaque integrity [17]. Excessive MMP activity, together with TF expression and persistent T cell activation, creates a highly unstable lesion prone to rupture.

Rupture exposes thrombogenic plaque contents, generating prothrombotic stimuli that accelerate thrombin formation through TF, von Willebrand factor, and subendothelial collagen, whose expression is upregulated by IL-1, TNF-α, and CD40L. Platelet adhesion and aggregation ensue, amplifying inflammation and driving acute complications such as myocardial infarction [8].

## 3. Contribution of Immune Cells to Atherosclerosis

Immune cells orchestrate both the progression and modulation of atherosclerosis through complex interactions in the vascular microenvironment. Monocytes infiltrate the intima and differentiate into macrophages, which regulate cholesterol metabolism, drive foam cell formation, and sustain chronic inflammation [18,19]. Dendritic cells, though less abundant, are critical for antigen presentation and T cell activation, thereby linking innate and adaptive immunity [20].

Among T cell subsets, regulatory T cells (Tregs) exert anti-atherogenic effects by suppressing inflammation and stabilizing plaques, whereas Th1 cells, characterized by IFN-γ production, enhance vascular inflammation and lesion development [21]. NKT cells bridge innate and adaptive responses; their activation by lipid antigens promotes cytokine release and cytotoxic activity, contributing to lesion expansion [22,23]. B cells display dual roles: class-switched antibody–producing subsets

exacerbate atherosclerosis, while IgM-producing B1 cells provide protection [24]. Natural killer (NK) cells also demonstrate pro-atherogenic functions through perforin- and granzyme B–mediated cytotoxicity and necrotic core expansion, with experimental models confirming their role in plaque destabilization [25, 26].

The diverse contributions of these immune cells are summarized in **Table 1**, underscoring their multifaceted involvement in atherogenesis.

**Table 1. Immunological Aspects of Atherosclerosis**

| Immune cells | Key role in atherosclerosis |
|---|---|
| **Monocytes/macrophages** | Mediate foam cell formation, regulate cholesterol metabolism, sustain chronic inflammation [18,19] |
| **Dendritic cells** | Present antigens, activate naïve T cells, induce cytokine release [20] |
| **T cells** | Tregs suppress inflammation and stabilize plaques; Th1 cells promote IFN-γ–driven inflammation; NKT cells enhance cytokine release and lesion expansion [21-23] |
| **B cells** | Class-switched B cells are pro-atherogenic; IgM-producing B1 cells are protective [24] |
| **NK cells** | Promote plaque instability via perforin/granzyme B; NK cell depletion reduces lesions [25,26] |

## 4. Therapeutic Potential of Conventional Drugs in Atherosclerosis Control

**(i) Nifedipine:** Nifedipine, an L-type calcium channel blocker, exerts anti-atherosclerotic effects through multiple mechanisms. It enhances peroxisome proliferator-activated receptor-γ (PPARγ) activity in macrophages by inhibiting extracellular signal-regulated kinase 1/2 and PPARγ2-Ser112 phosphorylation, thereby promoting lipid efflux pathways [27,28]. Nifedipine also suppresses monocyte chemoattractant protein-1 (MCP-1) and induces ATP-binding cassette transporter A1 (ABCA1) expression in macrophages [29]. In apolipoprotein E–deficient mice, treatment reduced lesion size and MCP-1 expression while increasing ABCA1 expression [30]. Clinical studies further demonstrate that nifedipine restores endothelial function, attenuates vascular inflammation, and decreases coronary events, collectively slowing atherosclerotic progression [31].

**(ii) Ramipril:** Ramipril, particularly in combination with rosuvastatin, has been shown to reduce intima-media thickness (IMT) and plaque size more effectively than statin monotherapy [32]. Additionally, it lowers circulating high-sensitivity C-reactive protein (hs-CRP) levels, suggesting an anti-inflammatory role that may reduce cardiovascular risk [33].

**(iii) Perindopril:** Perindopril improves endothelial function and attenuates plaque progression [34]. In experimental models, low doses reduced atherosclerotic plaque formation in cholesterol-fed rabbits [35]. It also enhanced collagen and non-collagen synthesis by smooth muscle cells, limited lipoprotein binding, and mitigated lesion development [36]. Clinically, perindopril has been associated with improved blood pressure profiles and favourable outcomes in patients with hypertension and coronary atherosclerosis undergoing revascularization [37].

## 5. Therapeutic Potential of Natural Products in Atherosclerosis Control

**(i) Flaxseed-Derived Compounds:** Flaxseed is rich in α-linolenic acid and lignans, particularly secoisolariciresinol diglucoside (SDG) and flax lignan complex (FLC). SDG levels range between 0.6–1.8 g/100 g of seed, while FLC typically contains 34–38% SDG, 15–21% cinnamic acid glucoside, and 9.6–11% hydroxymethyl glutaric acid [38,39].

SDG exhibits both anti-hyperlipidemic and anti-oxidative effects, contributing to the attenuation of atherosclerosis. In hypercholesterolemic rabbit models, SDG reduced lesion progression by 24% after 2 months and by 45% after 4 months of supplementation, with extended treatment achieving 17.5% lesion regression [40,41]. The benefits were linked to lowered oxidative stress rather than lipid reduction, as cholesterol-fed animals switched to normal diet paradoxically developed accelerated

atherosclerosis. These findings indicate that SDG primarily slows disease progression and, with prolonged use, promotes partial regression through antioxidant mechanisms.

FLC supplementation slowed lesion progression by approximately 31–32% in hypercholesterolemic animal models, an effect accompanied by reduced oxidative stress markers [42,43]. However, it did not induce significant regression of established lesions. Mechanistic studies suggest that the protective role of FLC may involve antioxidant properties, lipid-lowering effects, guanylate cyclase stimulation, nitric oxide donation, and reductions in vascular cholesterol and smooth muscle cell accumulation [44,45].

**(ii) *Sphaeranthus indicus*:** *Sphaeranthus indicus* (Asteraceae), a traditional Ayurvedic herb, contains diverse bioactive compounds including sesquiterpene lactones such as 7-hydroxyfrullanolide (7-HF). Extracts demonstrate anti-inflammatory and anti-hyperlipidemic properties relevant to atherosclerosis [46].

- **Anti-inflammatory effects.** Methanolic extracts and 7-HF suppress pro-inflammatory cytokine production and inhibit adhesion molecule expression (VCAM-1, ICAM-1, E-selectin) via NF-κB pathway modulation. In vivo, extracts reduced aortic lesion size in hyperlipidemic mice and hamsters without altering lipid profiles, suggesting an inflammation-driven mechanism [47].
- **Antihyperlipidemic activity.** In rats fed an atherogenic diet, administration of *S. indicus* extract (500 mg/kg/day) reduced total cholesterol, LDL-c, triglycerides, and body weight while increasing HDL-c. The extract improved atherogenic index and lipid ratios, possibly through enhanced lecithin-cholesterol acyltransferase (LCAT) and lipoprotein lipase activity [48].

**(iii) Flavonoids:** Flavonoids, plant-derived polyphenols, exhibit antioxidant, anti-inflammatory, and endothelial-protective properties that collectively counteract atherosclerotic processes [49,50].

**(iii.a) Quercetin:** Quercetin exerts anti-atherogenic effects through activation of SIRT1 and AMPK pathways, leading to reduced oxidative stress, inflammation, and endothelial dysfunction [51,52]. It inhibits dendritic cell activation, attenuates vascular senescence, and decreases plaque inflammation in animal models [53]. Supplementation reduces aortic lesions, modulates lipid metabolism, and prevents acute aortic syndromes in hypercholesterolemic animals [54,55].

**(iii.b) Anthocyanins:** Anthocyanins enhance antioxidant defences, activate Nrf2-regulated genes, and reduce inflammatory signalling [56,57]. Protocatechuic acid, a major metabolite, inhibits monocyte adhesion via NF-κB suppression [58]. Animal studies demonstrate improved HDL function, reduced aortic cholesterol, and protection against hypercholesterolemia-induced oxidative stress [59-61]. Effects appear source-dependent, with some reports indicating variable impact on lipid profiles [62,63].

**(iii.c) Biochanin A:** Biochanin A (BCA), an isoflavone, improves lipid profiles by elevating HDL-c and lowering LDL-c and total cholesterol, while suppressing pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) [64,65]. In apoE$^{-/-}$ mice, BCA reduced lesion size, improved reverse cholesterol transport, and inhibited foam cell formation by decreasing intracellular cholesterol accumulation [66].

**(iii.d) Baicalin:** Baicalin, isolated from *Scutellaria baicalensis*, exhibits antioxidant, immunomodulatory, and lipid-regulating activities. It inhibits foam cell formation, suppresses TLR4 and iNOS expression, and promotes anti-inflammatory signalling [67,68]. Network pharmacology and experimental studies identified NOX4 as a key target mediating its antioxidative effects, suggesting novel mechanisms for baicalin in atherosclerosis therapy.

**Table 2.** Clinical trials involving natural antioxidant compounds

| Antioxidant | Study Design | Results | Conclusion and Reference |
|---|---|---|---|
| **Vitamin E** | • A cohort of 87,245 female nurses<br>• Without prior cancer or cardiovascular disease | • 552 severe CAD cases reported.<br>• Women with the highest vitamin E intake showed | • Vitamin E supplementation may lower CAD risk in women aged 34–59 [69]. |

| | | | |
|---|---|---|---|
| | | a relative risk (RR) of 0.66.<br>• Short-term supplementation showed little effect, while >2 years of supplementation reduced risk (RR = 0.59). | |
| **Quercetin** | • 93 overweight or obese subjects.<br>• Received either 150 mg/day quercetin or placebo for 6 weeks. | • Quercetin reduced SBP by 2.6 mmHg and decreased serum HDL-C levels.<br>• Ratios of total cholesterol, TAG/HDL-C, and LDL/HDL-C remained unchanged.<br>• Plasma oxidized LDL decreased.<br>• CRP and TNF-α unaffected. | • Quercetin may help reduce SBP and oxidized LDL, indicating a protective role in CVD [70]. |
| **EGCG** | • 35 age and sex matched obese patients with metabolic syndrome<br>• Green tea (4 cups/day), control (4 cups water/day), or green tea extract (2 capsules + 4 cups water/day) for 8 weeks.<br>• EGCG doses were similar across tea and extract groups. | • Both green tea and extract groups showed significant weight reduction.<br>• Green tea also reduced LDL-C and LDL/HDL ratio<br>• Significantly lowered lipid peroxidation markers (HNE and MDA). | • Green tea reduces body weight and lipid peroxidation<br>• Suggests a beneficial role in improving metabolic syndrome [71]. |
| **Resveratrol** | • 66 patients with metabolic syndrome.<br>• Received 150 mg/ day resveratrol, 1,000 mg/day resveratrol, or placebo for 16 weeks. | • No reduction in the plasma levels of soluble urokinase plasminogen activator receptor, hs-CRP, or IL-6.<br>• No change in the expression of inflammatory genes in fat and muscle tissues.<br>• No beneficial effect on lipid or glucose metabolism.<br>• Up-regulated the levels of total cholesterol, LDL C and fructosamine. | • Resveratrol had no beneficial effect on blood glucose homeostasis, inflammatory state, blood pressure or liver lipid content in patients with MetS.<br>• Resveratrol (high dose) up-regulated the levels of total cholesterol, LDL-C and fructosamine [72] |
| **Probucol** | • 303 patients with hypercholesterolemia were assigned to receive placebo or probucol combined with dietary | • Probucol treated patients reduced their total cholesterol by 15% and HDL-C by 35%. | • Probucol provides obvious protection against Cu2+ catalyzed LDL oxidation. |

| | | | |
|---|---|---|---|
| | recommendations and cholestyramine for 3 years | • The LDL was more resistant to the Cu2 +- induced oxidation.<br>• Probucol has no significant effect on the progression and regression of femoral atherosclerosis. | • Probucol do not affect the development of femoral atherosclerosis [73]. |
| **lycopene** | • 175 Healthy male subjects recruited.<br>• Received supplements of lycopene (15 mg), lutein (15 mg), β carotene (15 mg), or placebo every day for 3 months. | • Supplementation of β-carotene, lycopene, and lutein resulted in an obvious increase in plasma and LDL of these carotenoids.<br>• The levels of other carotenoids in plasma or LDL did not change.<br>• The supplement failed to enhance LDL antioxidant capacity or change the ratio polyunsaturated/ of saturated fatty acids. LDL | • No beneficial or adverse effects of supplementation of β carotene, lycopene or lutein, on oxidative stress observed biomarkers were observed [74]. |

**Table 2.** Describes the clinical research design, number of cases, trial results, and conclusions of research on some of the natural products.
**Abbreviations**: CAD: Coronary artery disease; CVD: Cardiovascular disease; CRP: C-reactive protein; EGCG: Epigallocatechin-3-gallate; HDL-C: High density cholesterol; HNE: Hydroxynonenals; hs-CRP: High-sensitivity C-reactive protein; LDL-C: Low density cholesterol; MDA: Malondialdehyde; MetS: Metabolic syndrome; SBP: Systolic blood pressure; TAG: Triacylglyceride;

**6. Soluble Ninjurin-1 as a Potential Anti-Inflammatory Agent in Atherosclerosis**

Ninjurin-1 (Ninj1), also known as nerve injury-induced protein 1, has recently been identified as a substrate of matrix metalloproteinase-9 (MMP9) in plaque macrophages. Elevated levels of its soluble form (sNinj1) have been detected in the serum of patients with coronary artery disease. Jeon et al. (2020) [75] investigated the role of Ninj1 in atherosclerosis and reported that Ninj1 cleavage by MMP9 releases sNinj1, which exhibits anti-inflammatory properties. Within atherosclerotic lesions, Ninj1 expression was predominantly localized to alternatively activated macrophages (AAMs), a subset with anti-inflammatory activity.

Their findings indicated that Ninj1 plays a crucial role in maintaining immune balance by suppressing arterial inflammation. Deletion of Ninj1 aggravated inflammatory responses and accelerated atherosclerosis in mouse models, whereas administration of sNinj1 or synthetic peptides mimicking its function reduced inflammation and improved disease outcomes. Mechanistic studies revealed that Ninj1 inhibits pro-inflammatory pathways such as MAPK while simultaneously enhancing anti-inflammatory signalling through PI3K/Akt. Sustained treatment with sNinj1 analogues consistently attenuated inflammation and disease progression without adverse effects. Collectively, these observations highlight the therapeutic potential of targeting Ninj1 processing or mimicking its soluble form as a novel strategy to manage atherosclerosis.

**7. Canakinumab:** Canakinumab, a fully human monoclonal antibody targeting interleukin-1β (IL-1β), has been evaluated for its role in reducing inflammation-driven cardiovascular risk. The

Canakinumab Anti-inflammatory Thrombosis Outcomes Study (CANTOS) (NCT01327846) is a randomized, double-blind, placebo-controlled, event-driven Phase III study designed to evaluate the efficacy, safety and tolerability of quarterly subcutaneous injections of ACZ885 (also known as canakinumab) in combination with standard of care in the prevention of recurrent cardiovascular (CV) events. Results from the CANTOS trial demonstrated a significant reduction in cardiovascular events among patients with a prior history of myocardial infarction, independent of changes in lipid levels or blood pressure [76,77]. The drug functions by binding specifically to IL-1β, forming an antigen–antibody complex that prevents IL-1β from interacting with its receptor IL-1R1, thereby blocking downstream IL-1 signalling. This selectivity minimizes interference with other IL-1 family cytokines, potentially lowering adverse effects such as infection risk. Structural modelling studies using Protein Data Bank (PDB) data confirmed that the Fab fragment of canakinumab overlapped with the D1 domain of IL-1R1, effectively blocking IL-1β from receptor engagement [78].

Further investigations assessed canakinumab's effect on superficial femoral artery (SFA) plaque burden in patients with peripheral artery disease (PAD) over a 12-month period using high-resolution 3.0T MRI. Although no significant changes in SFA plaque size were noted between treatment and placebo groups, exploratory endpoints revealed early improvements in both maximum and pain-free walking distances among canakinumab-treated patients. This effect may reflect enhanced skeletal muscle perfusion or improved endothelial function, independent of plaque regression. Additionally, treatment significantly reduced circulating interleukin-6 (IL-6), reinforcing its systemic anti-inflammatory action. Interestingly, the differential impact on pain-free versus maximum walking distance suggests possible modulation of pain signalling, potentially by reducing ischemia-induced lactate accumulation. In line with CANTOS, the study highlighted that patients with elevated baseline high-sensitivity C-reactive protein represented a high-inflammatory burden population that could particularly benefit from IL-1β inhibition.

## 8. Conclusion

Atherosclerosis is a multifactorial disorder and continues to be a major global cause of death due to its association with cardiovascular events such as coronary artery disease, myocardial infarction, and stroke. Its pathogenesis involves a complex interaction of lipid deposition, immune-inflammatory mechanisms, and diverse risk factors, highlighting the need for multidimensional therapeutic strategies. This review emphasized the influence of both classical risk factors—including elevated LDL cholesterol, hypertension, and smoking—and non-traditional contributors such as poor sleep quality, sedentary lifestyle, and environmental stress.

The therapeutic landscape is shifting toward a combination of conventional drugs and natural product–based interventions. Plant-derived compounds like secoisolariciresinol diglucoside (SDG) and flaxseed lignans (FLC) have shown potential in lowering lipid levels and attenuating inflammation. Likewise, the anti-inflammatory effects of biologics such as canakinumab, along with medicinal plants like *Sphaeranthus indicus*, provide additional treatment opportunities. Flavonoids such as quercetin and anthocyanins, as well as novel molecular targets like Ninjurin-1 (NINJ1), further expand therapeutic possibilities by modulating oxidative stress and immune responses.

Established pharmacological treatments, including antihypertensive drugs such as nifedipine, ramipril, and perindopril, remain central to reducing cardiovascular risk. However, combining these with natural product–based therapies may yield synergistic effects, improving both efficacy and patient outcomes.

Overall, this review highlights the importance of adopting a holistic approach to atherosclerosis management, taking into account its multifactorial nature and the need for tailored treatment strategies. Future investigations should continue to unravel the molecular mechanisms driving atherosclerosis and evaluate the therapeutic promise of both conventional and novel agents. By broadening our understanding and expanding available interventions, we can advance the fight against atherosclerosis and enhance cardiovascular health on a global scale.

**Acknowledgements**
The authors are grateful to University of Lucknow, Lucknow and Indira Gandhi National Open University, New Delhi for providing basic infrastructure required to carry out the review process.

**Consent for publication**
Not applicable

**Competing interests**
All the authors declare that there are no competing interests.

**Funding**
The work was not funded by any funding agencies.

**Authors' contributions**
VKS and PS; Collected the primary data and wrote the paper. PKS: Designed the study, analysed the data, and wrote the manuscript. All authors have read and approved the final manuscript.

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