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From Tradition to Therapy: Medicinal Plants as a Promising Approach to Atherosclerosis

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ABSTRACT

Atherosclerosis, a major cardiovascular disease, is characterized by the accumulation of fatty streaks and plaques in arterial walls, driven by factors such as inflammation, oxidative stress, and lipid buildup. This review explores the therapeutic potential of medicinal plants as a promising option for preventing and managing atherosclerosis, emphasizing their bioactive compounds that target key disease mechanisms. Plants such as *Perovskia abrotanoides*, rich in phenolic compounds and essential oils, exhibit antioxidant and anti-inflammatory properties that mitigate oxidative stress and vascular damage. Similarly, widely accessible plants like ginger, turmeric, and garlic offer cardiovascular benefits by reducing inflammation and preventing arterial fat accumulation when incorporated into daily diets. This article extends its focus to additional medicinal plants, including *Gundelia tournefortii*, *Pulicaria gnaphalodes*, *Valeriana officinalis*, *Sesamum indicum*, *Allium ampeloprasum*, and *Origanum majorana*, which demonstrate significant anti-atherosclerotic effects. These plants contribute through diverse mechanisms, such as improving lipid profiles, inhibiting LDL oxidation, enhancing endothelial function, and reducing pro-inflammatory cytokines. The review highlights the limitations of synthetic drugs, including side effects and costs, underscoring the resurgence of interest in natural remedies. By integrating traditional knowledge with modern research, this study elucidates the molecular pathways—such as modulation of lipid metabolism and reduction of foam cell formation—through which these plants act. While preliminary findings are promising, further in vivo studies are needed to validate

efficacy and safety. This comprehensive analysis aims to develop strategies for leveraging medicinal plants as viable, accessible options for atherosclerosis management, promoting cardiovascular health and overall wellness.

Keywords: Atherosclerosis, Medicinal Plants, Cardiovascular Diseases, *Perovskia abrotanoides*, Phytotherapy

1. INTRODUCTION

Atherosclerosis is one of the most significant cardiovascular conditions, affecting arteries through the formation of fatty streaks and plaques. By influencing the contributing factors, plant-based compounds can aid in the treatment or prevention of atherosclerosis [1]. This disease is the most prevalent and important cardiac condition, involving the heart and brain. It progresses slowly and is a leading cause of mortality, beginning in childhood and manifesting clinically in adulthood [2].

Atherosclerosis is an inflammatory vascular disease characterized by the progressive accumulation of cholesterol in arterial walls, making it a major cause of cardiovascular disease. Issues related to the side effects of synthetic drugs have recently led to drug misuse, lack of patient consultations, and disruptions in disease control. Consequently, there has been a renewed interest in medicinal plants, with extensive research conducted to develop novel naturally based drugs [3].

This disease is a major cause of death and disability in developing countries. The most important risk factors include excessive fat consumption, low physical activity, and high blood cholesterol levels. These factors lead to functional and structural disorders of the vascular wall [4]. High concentrations of blood plasma cholesterol, primarily in the form of low-density lipoprotein (LDL), are considered the main cause of atherosclerosis. Research has shown that oxidized LDL (ox-LDL) represents the first stage of atherosclerosis in cardiovascular diseases [5].

Perovskia abrotanoides Karel. (Lamiaceae) is an aromatic herb primarily grown in the mountains of Northeastern Iran, Northern Pakistan, and Northwestern India. A suitable system for regenerating *P. abrotanoides* via direct organogenesis was recently developed for the first time [5].

Atherosclerosis is a chronic inflammatory disease characterized by the accumulation of lipids, cholesterol, and inflammatory cells within arterial walls, leading to plaque formation. These plaques can restrict blood flow, causing severe cardiovascular complications such as heart attacks and strokes. The disease is influenced by a combination of genetic, environmental, and lifestyle factors, including poor diet, lack of physical activity, smoking, and stress [6].

Recent studies have highlighted the limitations of synthetic drugs in managing atherosclerosis, particularly due to their side effects and high costs.

This has led to a renewed interest in natural remedies, especially medicinal plants, which offer a safer and more affordable alternative. Medicinal plants contain bioactive compounds such as polyphenols, flavonoids, and terpenoids, which have been shown to modulate lipid metabolism, reduce oxidative stress, and inhibit inflammation—key processes involved in the development of atherosclerosis [7].

2. ATHEROSCLEROSIS

Atherosclerosis is a complex disease involving multiple cellular and molecular mechanisms. The initial stage involves endothelial dysfunction, where the inner lining of arteries becomes damaged due to factors such as high blood pressure, smoking, or high cholesterol levels. This damage triggers the recruitment of immune cells, particularly monocytes, which differentiate into macrophages and engulf oxidized LDL (ox-LDL) particles, forming foam cells. These foam cells accumulate in the arterial wall, leading to the formation of fatty streaks, the earliest visible sign of atherosclerosis. As the disease progresses, smooth muscle cells migrate to the site of injury, producing extracellular matrix components that contribute to plaque stability. However, unstable plaques can rupture, leading to thrombus formation and acute cardiovascular events. Recent research has emphasized the role of chronic inflammation in atherosclerosis, with inflammatory markers like C-reactive protein (CRP) being strong predictors of disease progression [8].

Atherosclerosis is a multifocal, smoldering, immunoinflammatory disease of medium-sized and large arteries fueled by lipids. Endothelial cells, leukocytes, and intimal smooth muscle cells are the major players in the development of this disease [9].

The risk of developing atherosclerosis is no longer concentrated in Western countries and is now a leading cause of death worldwide. Atherosclerosis affects younger individuals, more women, and people from diverse ethnic backgrounds than previously observed. Recent research has also focused on triglyceride-rich lipoproteins, in addition to LDL, as causal factors in atherosclerosis. Medicinal plants have shown potential in interacting with these or other pathogenesis factors to prevent atherosclerosis [10].

Elevation in markers of inflammation predicts outcomes in patients with acute coronary syndromes, independent of myocardial damage. Additionally, low-grade chronic inflammation, as indicated by levels of the inflammatory marker CRP, prospectively defines the risk of atherosclerotic complications, adding to the prognostic information provided by traditional risk factors [11]. Recent advances in basic science have established a fundamental role for inflammation in mediating all stages of atherosclerosis, from initiation through progression and, ultimately, thrombotic complications [11].

Research on the functions of non-coding RNAs in plaque development has improved, showing that microRNAs (miRNAs) and long non-coding RNAs (lncRNAs) alter the transcription of genes implicated in atherosclerosis [12]. Atherosclerosis, the primary cause of coronary artery disease (CAD) and stroke, is a disorder with multiple genetic and environmental contributions [13]. Glycation of collagen may also promote atherogenesis [14].

3. PROPERTIES OF *PEROVSKIA ABROTANOIDES*

Perovskia abrotanoides, commonly known as Russian sage, is a medicinal plant with a wide range of therapeutic properties. It is rich in phenolic compounds, flavonoids, and essential oils, which contribute to its antioxidant, anti-inflammatory, and antimicrobial activities. The plant has been traditionally used in Iranian and Pakistani folk medicine to treat various ailments, including cardiovascular diseases, liver disorders, and infections [15].

Recent studies have shown that the essential oil extracted from *P. abrotanoides* contains compounds like camphor, 1,8-cineole, and α -pinene, which exhibit strong antioxidant

properties. These compounds help neutralize free radicals, reducing oxidative stress—a key factor in the development of atherosclerosis. Additionally, *P. abrotanoides* has been found to inhibit protein aggregation, which may play a role in preventing the formation of advanced glycation end products (AGEs) that contribute to vascular damage [16].

P. abrotanoides grows in sandy-textured soils with natural pH and low electrical conductivity. Regression analysis between climatic variables and growth periods showed that 96% of the variation in plant growth can be explained by altitude, precipitation, and temperature. Temperature had the highest effect on *P. abrotanoides* growth compared to other parameters [17]. The essential oil extracted from the stems and leaves of *P. abrotanoides* is a promising source of natural products with potential antioxidant and antimicrobial activities [18].

The root extract of *P. abrotanoides* has been shown to inhibit protein aggregation in a concentration-dependent manner due to its interaction with the hydrophobic areas of proteins [19]. This plant is also used for the treatment of leishmaniasis [20] and is a medicinally important plant found in Baluchistan province and northern areas of Pakistan. Local communities use it to treat typhoid, headaches, gonorrhea, vomiting, motion sickness, toothaches, atherosclerosis, cardiovascular diseases, liver fibrosis, and cough [21–22].

Additionally, *P. abrotanoides* has demonstrated anti-bladder carcinoma activity, reducing the viability of malignant bladder cell lines in a dose-dependent manner [23].

4. USES OF *PEROVSKIA ABROTANOIDES*

In traditional medicine, *P. abrotanoides* has been used as a natural remedy for rheumatic pain, fever, and headaches. Its antimicrobial properties make it effective against a range of pathogens, including bacteria and fungi. The plant's essential oil has shown significant inhibitory activity against microbial strains, making it a potential candidate for developing natural antibiotics [24].

The plant is used in Iranian folk medicine as an analgesic for rheumatic pain and for the treatment of leishmaniasis, fever, and headaches. Rural healers have used it as a tonic, antiseptic, anti-inflammatory, and treatment for leishmaniasis, often in combination with other medicinal plants [25]. The essential oil extracted from *P. abrotanoides* has demonstrated high antimicrobial activity against five microbial strains, with inhibition zones of up to 18 mm [26]. Hairy root cultures of *P. abrotanoides* have also been shown to produce tanshinones and phenolic acids, making them a promising tool for large-scale production [27].

Essential oils from *P. abrotanoides* have shown effective antimicrobial activity at low concentrations, particularly during full flowering and seed setting [28]. An *n*-hexane extract of *P. artemisioides* aerial parts has demonstrated excellent capabilities in inhibiting biofilm formation by Gram-positive and Gram-negative pathogens and blocking cell metabolism within microbial biofilms [29].

Perovskia species possess therapeutic properties and have the potential to serve as viable alternatives to synthetic antioxidants in the food industry [30].

The root extract of *P. abrotanoides* has been confirmed to have antiglycative and antiglycotoxic potential, supporting its traditional use in diabetes management. The high activity can be attributed to the abundance of rosmarinic acid [31].

5. ROLE OF OTHER MEDICINAL PLANTS IN ATHEROSCLEROSIS

Gundelia tournefortii, commonly known as tumble thistle, is a medicinal plant with well-documented antioxidant and anti-atherosclerotic properties. It is rich in bioactive compounds such as coumarins, flavonoids, and terpenoids, which contribute to its therapeutic effects. These compounds have been shown to reduce total cholesterol and LDL cholesterol levels while increasing high-density lipoprotein (HDL) cholesterol, thereby improving the lipid profile [32]. Additionally, *G. Tournefortii* inhibits the oxidation of LDL particles, a critical step in the formation of atherosclerotic plaques. Oxidized LDL is more likely to be absorbed by macrophages, leading to foam cell formation and plaque development. Recent studies have also highlighted its anti-inflammatory properties, which help reduce vascular inflammation and endothelial dysfunction, both of which are key contributors to atherosclerosis [33]. Furthermore, *G. Tournefortii* has been found to enhance the activity of antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (GPx), providing additional protection against oxidative stress [34].

Pulicaria gnaphalodes is another medicinal plant with significant antioxidant and anti-inflammatory properties. It contains high levels of phenolic compounds, tannins, and anthocyanins, which are known to scavenge free radicals and reduce oxidative stress [35]. These compounds also inhibit the formation of foam cells by preventing the uptake of oxidized LDL by macrophages, a key step in the development of atherosclerotic plaques. Recent research has demonstrated that *Pulicaria gnaphalodes* extracts can reduce the expression of pro-inflammatory cytokines such as TNF- α and IL-6, further highlighting its potential in managing atherosclerosis [36]. Additionally, the plant has been shown to improve endothelial function by enhancing nitric oxide (NO) production, which helps maintain vascular tone and prevent endothelial dysfunction [37].

Valeriana officinalis, commonly known as valerian, is widely recognized for its vasorelaxant effects, which are primarily mediated by its ability to relax smooth muscle cells in the arterial walls. The root extract of this plant contains bioactive compounds such as valerenic acid and hesperidin, which have been shown to improve blood flow and reduce blood pressure [38]. Recent studies have also demonstrated that *Valeriana officinalis* enhances endothelial function by increasing the bioavailability of nitric oxide (NO), a key molecule that regulates vascular tone and prevents endothelial dysfunction [39]. Furthermore, valerian has been found to reduce oxidative stress by scavenging free radicals and enhancing the activity of antioxidant enzymes such as catalase and superoxide dismutase (SOD) [40]. These properties make *Valeriana officinalis* a valuable natural remedy for managing hypertension and atherosclerosis.

Sesamum indicum, or sesame, is a nutrient-rich plant whose seeds are packed with bioactive compounds such as lignans (e.g., sesamin and sesamol) and phenolic acids. These compounds exhibit potent antioxidant and anti-inflammatory properties, which are crucial in combating atherosclerosis [41]. Sesame lignans have been shown to reduce LDL cholesterol levels and inhibit the oxidation of LDL particles, thereby preventing the formation of atherosclerotic plaques [42]. Additionally, sesame seeds contain sesamol, a phenolic compound that further enhances their antioxidant capacity by scavenging free radicals and reducing oxidative stress [43]. Recent studies have also highlighted the role of sesame in improving endothelial function

by enhancing nitric oxide (NO) production and reducing the expression of adhesion molecules such as ICAM-1 and VCAM-1, which are involved in the recruitment of inflammatory cells to the arterial wall [44].

Allium ampeloprasum, commonly known as leek, belongs to the Alliaceae family and is rich in sulfur-containing compounds such as allicin and diallyl disulfide. These compounds are known for their strong antioxidant and anti-inflammatory effects, which help reduce oxidative stress and improve lipid profiles [45]. Leeks also contain flavonoids and other bioactive molecules that enhance the activity of antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (GPx) [46]. By reducing oxidative damage to vascular tissues and improving lipid metabolism, *Allium ampeloprasum* plays a significant role in preventing the development and progression of atherosclerosis. Recent studies have also demonstrated that leek extracts can reduce blood pressure and improve endothelial function by enhancing nitric oxide (NO) bioavailability [47]. These properties make leek a valuable addition to an anti-atherosclerotic diet.

Origanum majorana, or marjoram, is a herb rich in phenolic compounds such as carvacrol and thymol, which are known for their strong antioxidant properties. These compounds help maintain a balance between free radical production and the body's antioxidant defenses, thereby reducing oxidative stress—a key contributor to atherosclerosis [48]. Marjoram also inhibits the formation of foam cells by preventing the uptake of oxidized LDL by macrophages [49]. Additionally, its anti-inflammatory properties help reduce vascular inflammation, which is a critical factor in the progression of atherosclerotic plaques. Recent studies have shown that marjoram extracts can reduce the expression of pro-inflammatory cytokines such as TNF- α and IL-6, further highlighting its potential in managing atherosclerosis [50]. The combination of these effects makes *Origanum majorana* a promising natural remedy for cardiovascular health and the prevention of atherosclerosis.

6. CONCLUSION

A critical analysis of the current literature demonstrates that the accumulated knowledge of traditional herbal medicine and modern approaches to studying the action of medicinal plants has unveiled the mechanisms of action and potential applications of plant-based preparations in managing atherosclerosis. Medicinal plants facilitate the treatment of atherosclerosis through various pathways and mechanisms of action. Several medicinal plants show promise for the prevention or treatment of atherosclerosis, but more in vivo studies are recommended to validate their efficacy and safety.

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