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Phytochemical Constituents and Therapeutic Potential of Pine Bark and Needle Extracts in Cardiovascular and Metabolic Disorders

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Abstract — Cardiovascular and metabolic diseases remain leading global health challenges, necessitating novel and complementary therapeutic strategies. Natural plant-derived compounds, particularly from pine bark and needles, have attracted attention for their potential health benefits. This study aims to comprehensively review the phytochemical composition of pine bark and needle extracts, focusing on their biological activities and potential roles in preventing and managing cardiovascular and metabolic disorders. A literature review was conducted using databases such as PubMed, ScienceDirect, and Google Scholar, focusing on studies published from 2000 to 2024. The selection criteria included in vitro, in vivo, and clinical research articles investigating the phytochemical profiles and pharmacological effects of pine bark and needle extracts on cardiovascular and metabolic health. Pine bark and needle extracts, especially from Pinus pinaster, are rich in proanthocyanidins, flavonoids, phenolic acids, stilbenes, and terpenoids. These bioactive compounds exhibit potent antioxidant, anti-inflammatory, and endothelial protective properties. Clinical and preclinical studies demonstrate improvements in blood pressure, lipid profiles, glucose metabolism, and vascular function. Emerging evidence also suggests a role in modulating gut microbiota, contributing to systemic metabolic benefits. Pine bark and needle extracts hold significant promise as adjunct therapies for cardiovascular and metabolic diseases through their multi-targeted mechanisms. Further well-designed clinical trials are necessary to validate their efficacy, optimize dosages, and ensure safety for broader therapeutic application.

Keywords *— pine bark extract; pine needle extract; cardiovascular diseases; metabolic syndrome, phytochemicals.*

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INTRODUCTION

Cardiovascular and metabolic disorders, including hypertension, dyslipidemia, type 2 diabetes mellitus (T2DM), and metabolic syndrome, remain leading causes of morbidity and mortality worldwide [1]. These conditions are characterized by complex pathophysiological mechanisms involving oxidative stress, chronic inflammation, endothelial dysfunction, and insulin resistance. The increasing prevalence of these disorders underscores the urgent need for effective preventive and therapeutic strategies [6].

Cardiovascular diseases (CVDs) remain a leading cause of mortality globally and impose a substantial economic burden on healthcare systems. Despite significant progress in prevention and treatment, the persistence of harmful lifestyle habits and adverse environmental exposures continues to hinder these advances, leading to an ongoing increase in global CVD-related deaths over the past three decades. The concurrent rise in metabolic disorders, along with upstream social determinants of health, shares overlapping pathophysiological mechanisms that accelerate CVD progression, thereby exacerbating its worldwide social and economic impact. Furthermore, the heterogeneous and multifactorial nature of CVDs shaped by cultural norms, genetic predispositions, socioeconomic conditions, and other region-specific determinants complicates efforts to implement uniform global strategies to tackle this burden effectively. While earlier research has focused on historical patterns of CVD prevalence

and mortality, the present study aims to utilize the latest epidemiological data to predict geospatial trends of CVD and its associated risk factors from 2025 to 2050. This includes a comprehensive analysis of metabolic, environmental, and behavioral contributors to CVD, while recognizing that new risk factors are continually being identified and influencing disease trajectories [7].

Pine bark extracts, particularly Pycnogenol® derived from *Pinus pinaster*, have garnered significant attention due to their rich content of bioactive compounds, including proanthocyanidins, flavonoids, and phenolic acids. These constituents exhibit potent antioxidant and anti-inflammatory properties, contributing to their therapeutic potential in managing cardiometabolic disorders. Clinical studies have demonstrated that Pycnogenol® supplementation can lead to improvements in endothelial function, reductions in systolic and diastolic blood pressure, and enhancements in lipid profiles among individuals with metabolic syndrome [1]. A systematic review and meta-analysis further confirmed that pine bark extract supplementation significantly reduces body weight, systolic blood pressure, low-density lipoprotein cholesterol, fasting blood sugar, and hemoglobin A1c levels, highlighting its role as an adjunct therapy in managing cardiometabolic risk factors [1].

Among conifers, the pine (*Pinus* L.) is a genus of more than 100 different species which grow widespread in Europe and the Mediterranean basin, Asia and in Northern America. Pine seeds, needles, cones and bark contain different categories of phytochemicals which are essential for plant growth and development as well as having protective functions for the pines [8]. Botanical extracts from pine bark have a long-standing history of use in traditional medicine, e.g., for wound healing [9]. Nowadays, they are still used as dietary supplements and insights into the scientific basis of their effects is yet increasing. Extracts can be sourced from different *Pinus* (*P.*) species such as *P. densiflora*, *P. maritima*, *P. massonia*, *P. nigra*, *P. pinaster*, *P. radiata*, or *P. sylvestris*. The bark extracts are concentrated sources of phenolic compounds such as procyanidins, flavonoids or phenolic acids. Their content and composition depend on the pine species and the precise extraction solvent and procedure. Therefore, the extract compositions are marked by different concentrations and types of phenolic compounds which account for individual bioactivities [10].

Pine needle extracts (PNEs) have also shown promising effects in addressing obesity and related metabolic disturbances. In animal models, PNE administration has been associated with decreased body weight, reduced fat mass, and improved glucose metabolism. Mechanistically, PNEs enhance hypothalamic proopiomelanocortin (POMC) neuronal activity, which plays a critical role in regulating energy balance and appetite [2]. Additionally, PNEs have been observed to suppress adipocyte differentiation and lipid accumulation by downregulating peroxisome proliferator-activated receptor gamma (PPARγ) expression, thereby mitigating obesity-related complications [2]. In WAT, PPARγ is pivotal to lipid accumulation. In contrast, PPARγ activation in BAT induces the expression of genes related to the thermogenic program, including *Pgc1α* and *Ucp1*. PPARγ is crucial for brown adipocyte differentiation, but additional transcription factors, including PRDM16, are required to activate the thermogenic program [11].

The therapeutic effects of pine bark and needle extracts are largely attributed to their diverse phytochemical profiles. These extracts are rich in flavonoids such as taxifolin, quercetin, and myricetin, as well as phenolic acids including caffeic and ferulic acids. These compounds exhibit strong antioxidant activities, scavenging reactive oxygen species and reducing oxidative stress, which is a key contributor to the pathogenesis of cardiovascular and metabolic diseases. Furthermore, the presence of stilbenes like piceatannol and astringin adds to the anti-inflammatory and cardioprotective properties of these extracts [3].

Recent studies have highlighted an emerging role of pine bark and needle extracts in modulating gut microbiota composition, which indirectly contributes to cardiovascular and metabolic health. Polyphenolic compounds from pine extracts, such as procyanidins and taxifolin, are metabolized by gut microbiota into bioactive metabolites that enhance gut barrier integrity, reduce systemic inflammation, and improve lipid metabolism. Furthermore, experimental models have demonstrated that pine-

derived flavonoids can attenuate vascular calcification by inhibiting oxidative stress-induced vascular smooth muscle cell (VSMC) transdifferentiation, offering a novel therapeutic approach in preventing atherosclerosis and arterial stiffness [5]. These findings suggest that pine bark and needle extracts not only exert direct antioxidant and anti-inflammatory effects but also influence host-microbiota interactions and vascular homeostasis, reinforcing their potential as multi-target agents in the management of cardiovascular and metabolic disorders [4].

Despite the promising findings, there is a need for more comprehensive clinical trials to fully elucidate the efficacy, optimal dosing, and safety profiles of pine bark and needle extracts in human populations. Future studies should focus on standardized extract preparations, long-term effects, and potential interactions with conventional therapies to better integrate these natural products into clinical practice.

MATERIALS AND METHOD

Study Approach

This study was conducted as a narrative review and phytochemical profiling analysis, aiming to provide an integrative overview of the bioactive constituents present in pine bark and needle extracts, as well as their therapeutic roles in cardiovascular and metabolic disorders. The approach combined literature synthesis, secondary data analysis, and mechanistic interpretation of existing experimental and clinical studies.

Data Collection

Scientific articles, original research papers, and reputable reviews published between 2014 and 2024 were retrieved from major scientific databases including PubMed, ScienceDirect, SpringerLink, and Google Scholar. Keywords used were: *"pine bark extract", "pine needle extract", "Pinus spp.", "phytochemical composition", "polyphenols", "cardiovascular disease", "metabolic syndrome", "antioxidant", and "anti-inflammatory effects"*. Additionally, authoritative phytochemical databases such as Dr. Duke's Phytochemical and Ethnobotanical Databases and PlantCyc were consulted for chemical constituent verification.

Selection Criteria

Studies were selected based on relevance to the following criteria, identification and quantification of bioactive compounds in pine bark and needles (e.g., procyanidins, flavonoids, phenolic acids, terpenoids), investigation of biological activities relevant to cardiovascular health (e.g., anti-inflammatory, antioxidant, vasodilatory effects), exploration of effects on metabolic parameters (e.g., lipid profile, insulin sensitivity, adiposity), studies focusing on non-cardiometabolic outcomes or unrelated plant species were excluded.

Data Analysis

The collected data were analyzed qualitatively. Phytochemical constituents were tabulated according to compound class (polyphenols, flavonoids, terpenoids, etc.), with emphasis on their biological mechanisms relevant to cardiovascular and metabolic disorders. Results from in vitro, in vivo, and human studies were comparatively analyzed to identify consistent patterns of therapeutic potential. Where available, molecular pathways modulated by pine-derived compounds (e.g., NF-κB, Nrf2, eNOS signaling) were discussed to elucidate underlying mechanisms of action.

Limitations

This study acknowledges limitations inherent to narrative reviews, including potential selection bias and lack of meta-analytic quantification. However, efforts were made to include the most recent and high-impact studies to ensure comprehensive coverage of the topic.

RESULTS AND DISCUSSION

Pinus pinaster Chemical Compound

Pinus pinaster is primarily composed of terpenoids and flavonoids (Sharma et al., 2018). Gas chromatography–mass spectrometry (GC–MS) analysis of its essential oil identified fifteen compounds, with α-pinene (60.80%), β-pinene (30.20%), camphene (1.0%), limonene (0.9%), α-terpineol (1.60%), and β-caryophyllene (1.10%) as the major constituents [13]. The essential oil derived from the wood of *Pinus pinaster* contains compounds such as α-thujene, caryophyllene, 3-carene, thunbergol, terpinolen, cambrene, α-caryophyllene, α-pinene, verticol, and sabinene. In contrast, the needle essential oil is rich in β-myrecene, α-pinene, terpinyl acetate, 3-carene, borneol acetate, α-terpineol, α-longipinene, and caryophyllene oxide [12]. The bark's essential oil predominantly includes α-pinene, camphene, cambrene, longifolene, thunbergol, sylvestrene, terpineol, terpinolen, D-limonene, terpinyl acetate, elemol, methyl dihydro abtate, myrcene, α-cadinol, β-pinene, eucalyptol, cis-carveol, cuminaldehyde, caryophyllene, eugenol, linalool, α-humulene, and α-terpineol in various amounts [14].

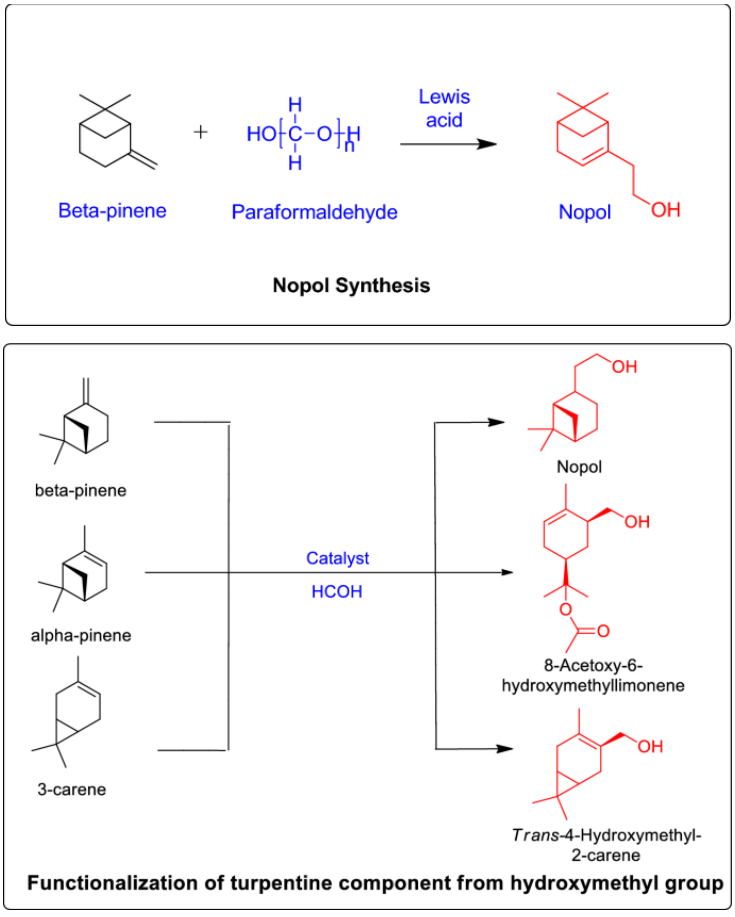

Fig. 1. Chemical Compound of *Pinus pinaster* [18].

GC–MS analysis of *Pinus pinaster* cone essential oil revealed the presence of α-humulene, caryophyllene, terpinene-4-ol, and δ-3-carene. Analyzed the hydrophilic extracts of the bark using gas chromatography, identifying sugars, sugar alcohols, pinoresinol, secoisolariresinol, catechin, gallocatechin, taxifolin, quercetin, and stilbenes [15]. The lipophilic fraction of the bark contained fatty acids along with diterpenoid acids such as abietic, pimaric, dehydroabietic, and neoabietic acid, with taxifolin found to be particularly abundant. GC–MS analysis of the ethyl acetate fraction of green needles detected primary compounds including octakis ether, methyloxime, and 3-α-mannobiose, whereas extracts from fallen needles were characterized by cyclodecasiloxane and eicosamethyl as major constituents [16]. Furthermore, the phytochemical constituents in *Pinus pinaster* bark extract included ellagic acid, octacosyl ferulate, methoxyprotocatechuate, 1,3,7-trihydroxyxanthone, ursolic acid, isopimaric acid, flavan-3-ol, 2,4,7-trihydroxyxanthone, taxifolin, quercetin, and isorhamnetin-3-O-rhamnoside [17].

Pharmacology

Pinus species offer a range of ecosystem services and play an important role in carbon sequestration, both in their biomass and soil [19]. Economically, these species are highly valuable across various industries. They are primarily prized for their high-quality timber, which serves as a critical raw material for wood products such as lumber, plywood, and particleboard, widely used in construction and furniture manufacturing [20]. Moreover, the long fibers found in pine wood make it a preferred resource for the paper and pulp sector [21]. Incorporating underutilized pine byproducts like bark, cones, and needles into particleboards can replace up to 20% of wood particles by weight, enhancing properties such as water resistance, internal bonding strength, and lowering formaldehyde emissions. This valorization of pine biomass has also been applied in the development of biomaterials [21].

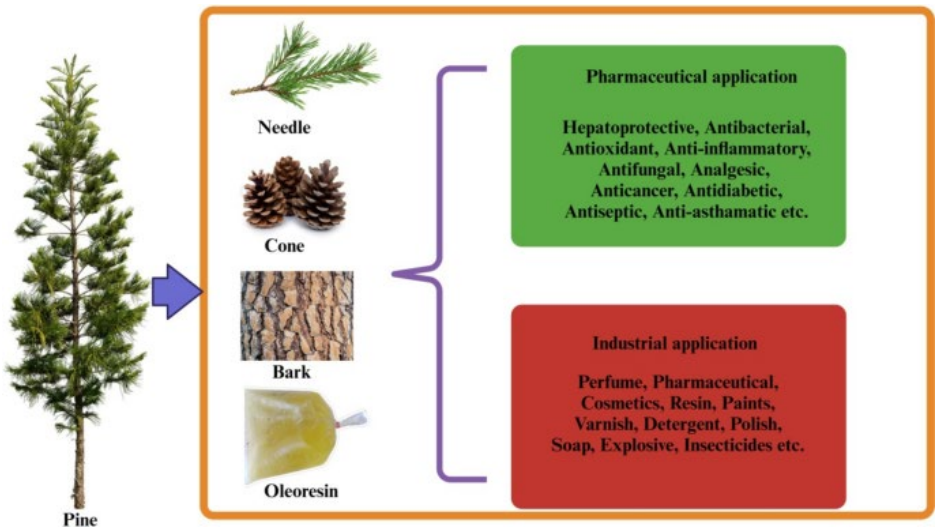

Fig. 2. Pharmacology of *Pinus pinaster* [18].

Certain Pinus species also produce oleoresin, which, after distillation, yields essential oil known as turpentine and a solid, non-volatile residue called rosin or colophony. Turpentine is primarily composed of monoterpenes, which have various industrial uses. For instance, borneol, a monoterpene found in Pinus, is utilized in cosmetic products [22]. Turpentine finds applications across pharmaceutical, perfume, and synthetic pine oil industries, among others [23]. Hydrocarbons derived from turpentine, such as bisabolene and β-caryophyllene, show promise as high-density biofuels through selective dimerization of pinenes. Hydrogenated turpentine is employed in producing bio-based jet fuels, offering an eco-friendly and sustainable energy alternative for the future [24].

Rosin and rosin acids exhibit multifunctional properties that make them suitable for use in varnishes, paints, detergents, cosmetics, soaps, rubber, paper, and polish manufacturing [25]. Additionally, rosin is utilized in the production of linoleum, explosives, insecticides, and disinfectants [26]. Beyond resin, pine trees also provide non-wood products such as needles, cones, and bark, which have applications in landscaping, biofuels, bioherbicides, and as substrates for plant cultivation [27].

Role of Extract Pine for Cardiovascular and Metabolic

Antioxidant Profile

Multiple studies have demonstrated that Pycnogenol acts as a potent free radical scavenger and antioxidant in vitro. Its ability to neutralize oxygen free radicals, including hydroxyl and superoxide radicals, was evaluated using an electron spin resonance spectrometer and compared with other well-known antioxidants such as *Ginkgo biloba* and green tea extracts. Vitamin C and vitamin E analogues served as reference compounds for hydroxyl radical scavenging, while superoxide dismutase (SOD) was used as the standard for superoxide radical scavenging activity [28]. In another investigation, murine macrophages stimulated with lipopolysaccharide (LPS) and interferon-gamma (IFN-γ) to induce nitric oxide synthase (NOS) expression revealed that Pycnogenol effectively scavenged hydroxyl, superoxide, and nitric oxide (NO) radicals [29]. It also prolongs the lifespan of the ascorbate radical and aids in regenerating vitamin E, while exhibiting stability against heat and ascorbate oxidase [28].

In two separate in vitro experiments, bovine vascular endothelial cells were pre-treated with Pycnogenol before being exposed to oxidative stress induced by t-butyl hydroperoxide (t-BHP). Cell death and lipid peroxidation were measured using lactate dehydrogenase (LDH) release and malondialdehyde (MDA) levels, respectively. Preincubation with Pycnogenol at concentrations between 10 and 80 μg/ml for 16 hours enhanced cell viability after t-BHP exposure and caused a dose-dependent reduction in MDA levels [30].

Another independent in vitro study utilized bovine retina tissue to assess Pycnogenol's ability to prevent lipid peroxidation, measured as thiobarbituric acid reactive substances (TBARS). Pycnogenol inhibited lipid peroxidation in a dose-dependent manner, showing significant effects even at 25 ng/ml and complete protection at 250 ng/ml. It was found to be more effective than standardized grape seed extract, ascorbate, α-tocopherol, and lipoic acid in this assay [31].

The antioxidant capacity of Pycnogenol was further validated in a separate laboratory using three different in vitro models involving oxidative burst, LDL oxidation, and an iron/ascorbic acid system as oxidative stress challenges. Pycnogenol inhibited the oxidative burst in J774 murine macrophages triggered by zymosan in a concentration-dependent manner. When co-incubated with copper sulfate, which induces oxidation of human plasma LDL (monitored by TBARS formation), Pycnogenol reduced LDL oxidation dose-dependently. Additionally, Pycnogenol significantly prevented strand breaks in pBR322 plasmid DNA caused by hydroxyl radicals generated by iron/ascorbic acid, as assessed by agarose gel electrophoresis [32].

Moreover, pretreatment of murine macrophages (RAW 264.7) with LPS increases the production of proinflammatory cytokines such as interleukin-1 beta (IL-1β). Pycnogenol treatment resulted in a dose-dependent decrease in these inflammatory mediators by inhibiting the activation of transcription factors NF-κB and AP-1, which regulate IL-1β production [34]. Furthermore, Pycnogenol treatment elevated intracellular levels of glutathione (GSH), glutathione peroxidase (GSH-Px), glutathione reductase (GSSG-R), superoxide dismutase (SOD), and catalase (CAT) per mg of protein, thereby enhancing the cell’s endogenous antioxidant defense system [33].

Chronic Venous Insufficiency and Deep Vein Thrombosis

Pycnogenol has demonstrated positive effects in managing chronic venous insufficiency (CVI). Several independent, double-blind clinical trials have reported statistically significant improvements in symptoms such as leg heaviness, swelling, and pain among patients treated with Pycnogenol. Among these symptoms, edema showed the most notable response to the treatment [35]. Additionally, two separate studies conducted on healthy travelers at risk of deep vein thrombosis (DVT) revealed that Pycnogenol, whether administered alone or in combination with other agents, provided beneficial outcomes [36]. Moreover, Pycnogenol supplementation has also shown effectiveness in patients suffering from venous ulcers [37]. Based on the understanding of DVT pathophysiology and motion sickness, as well as the biological activities of Pycnogenol and ginger extract, Scurr and Gulati developed a combination product called Zinopin [38]. Subsequent clinical studies involving travelers on long-haul flights demonstrated that Zinopin significantly reduced DVT symptoms and the incidence of motion sickness [38].

Hypertension

An 8-week supplementation regimen with Pycnogenol led to a significant decrease in systolic blood pressure, although diastolic pressure remained unchanged [39]. This effect likely relates to Pycnogenol's vasodilatory action through the stimulation of nitric oxide (NO) release by endothelial cells, which may alleviate stress-induced blood pressure elevation. In a placebo-controlled trial involving hypertensive patients who were already on nifedipine, a commonly prescribed antihypertensive drug, the addition of Pycnogenol allowed for a reduction in the dosage of nifedipine required to maintain blood pressure control. Analysis of blood samples from these patients showed an increase in vasodilatory factors NO and prostacyclin, along with a reduction in the vasoconstrictor endothelin-1 [40].

Diabetes and Diabetic Retinopathy

Both experimental and clinical studies support that diabetes is characterized by elevated blood levels of lipid peroxidation products, and oxidative stress plays a significant role in its pathogenesis [41]. Factors such as hyperglycemia, increased blood lipid levels, enhanced LDL oxidizability, compromised endogenous antioxidant defenses, and increased platelet aggregation contribute to diabetic complications, including retinopathy and cardiovascular diseases. Pycnogenol targets these pathological mechanisms, resulting in beneficial effects demonstrated in animal models and human clinical trials [42]. Specifically, Pycnogenol has been shown to reduce fasting and post-meal blood glucose levels in a dose-dependent manner while improving endothelial function by lowering endothelin-1 and raising blood levels of prostacyclin and NO [42]. These effects were confirmed in a placebo-controlled, double-blind study involving diabetic patients [43]. Furthermore, Pycnogenol has proven effective in treating diabetic retinopathy, evidenced by a significant reduction in capillary permeability in both eyes as measured by fluorescence angiography. A multicenter study conducted in Germany with 1,169 diabetic retinopathy patients found that six months of Pycnogenol treatment not only halted the progression of visual deterioration but also improved visual acuity in some cases. Additionally, Pycnogenol's ability to improve lipid profiles in diabetic individuals plays a critical role in systemic management of the disease [44].

CONCLUSION

Pine bark and needle extracts, particularly those derived from Pinus pinaster, present significant therapeutic potential in the management of cardiovascular and metabolic disorders. Rich in diverse phytochemicals such as proanthocyanidins, flavonoids, phenolic acids, stilbenes, and terpenoids, these extracts exert strong antioxidant and anti-inflammatory effects, mitigate endothelial dysfunction, and improve metabolic parameters including lipid profiles, blood pressure, and glucose metabolism. Furthermore, their emerging role in modulating gut microbiota and vascular homeostasis highlights their

multifaceted mechanisms of action. Despite encouraging findings from in vitro, in vivo, and clinical studies, further high-quality human trials are essential to establish standardized dosages, long-term efficacy, and safety profiles. Additionally, comprehensive investigations into potential interactions with conventional therapies are necessary to facilitate their integration into clinical practice. Overall, pine bark and needle extracts hold promise as valuable adjuncts in the prevention and treatment of cardiometabolic diseases, offering a natural, multi-targeted therapeutic approach.

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