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Systematic Review: The Effectiveness of Olive Oil on Oxidative Stress Process in the Development of Atherosclerosis

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Abstract. *This study aims to analyze the antioxidant effects of olive oil, particularly extra virgin olive oil (EVOO), in inhibiting oxidative stress and its role in the development of atherosclerosis. This study employed a systematic review approach by analyzing scientific articles published between 2020 and 2026 from databases such as PubMed, Scopus, Sinta, and Google Scholar. Selected studies examined the effects of olive oil and its bioactive compounds on oxidative stress, inflammation, and cardiovascular risk factors. The findings indicate that EVOO, especially its polyphenol content, plays a significant role in reducing reactive oxygen species (ROS), preventing LDL oxidation, improving endothelial function, and enhancing antioxidant enzyme activity. However, some studies reported inconsistent results depending on dosage, duration, and subject characteristics. Overall, EVOO demonstrates strong potential as a nutritional intervention to prevent and slow the progression of atherosclerosis through antioxidant, anti-inflammatory, and lipid-regulating mechanisms.*

Keywords: *Atherosclerosis, Olive Oil, Antioxidant, Oxidative Stress, Polyphenols*

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INTRODUCTION

Atherosclerosis is a chronic inflammatory disorder of the arterial wall that develops progressively over several decades and remains the principal pathological basis of atherosclerotic cardiovascular disease (ASCVD) (Frąk et al., 2022; Della et al., 2023; Młynarska et al., 2024; Gusev & Sarapultsev, 2023; Fularski et al., 2024). The disease is characterized by the accumulation of lipids within the arterial intima accompanied by persistent inflammatory responses that gradually lead to plaque formation, vascular remodeling, and narrowing of the arterial lumen. Unlike an acute condition, atherosclerosis evolves silently over time, often remaining asymptomatic until advanced lesions become unstable and precipitate life-threatening cardiovascular events (Bentzon et al., 2014; George, 2015; Nuotio et al., 2018; Williams, 2024; Tibaut et al., 2016). Consequently, atherosclerosis has become one of the leading global health concerns because of its high prevalence, long disease duration, and substantial contribution to cardiovascular morbidity and mortality.

The development of atherosclerosis is fundamentally driven by disturbances in lipid metabolism, particularly the retention and accumulation of low-density lipoprotein (LDL) cholesterol and remnant lipoprotein particles within the arterial wall (Sandesara et al., 2019; Ginsberg et al., 2021; Björkegren & Lusis, 2022; Jo, 2025; Wang et al., 2025). These lipoproteins undergo oxidative and enzymatic modifications that stimulate endothelial dysfunction and activate both innate and adaptive immune responses. The resulting inflammatory cascade

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promotes the recruitment of circulating monocytes into the subendothelial space, where they differentiate into macrophages and internalize modified lipids to form foam cells. This process initiates the formation of fatty streaks, which subsequently progress into fibrous plaques through continuous lipid deposition, extracellular matrix remodeling, and chronic inflammation. The inflammatory component of atherosclerosis is now recognized as an equally important determinant of disease progression alongside dyslipidemia. Rather than serving merely as a secondary response to lipid accumulation, inflammation actively regulates every stage of plaque development, including lesion initiation, progression, destabilization, and rupture.

Dri et al. (2023), Immanuel & Yun (2023), Kwaifa et al. (2020), Pacinella et al. (2022) said that, Numerous inflammatory mediators, including cytokines, chemokines, adhesion molecules, and matrix degrading enzymes, contribute to endothelial injury and vascular remodeling. Persistent activation of these inflammatory pathways weakens the fibrous cap covering the atherosclerotic plaque, thereby increasing its susceptibility to rupture and subsequent thrombus formation. This paradigm has shifted the understanding of atherosclerosis from a purely lipid storage disease toward a chronic inflammatory vascular disorder. Hemodynamic factors also play an important role in determining the localization of atherosclerotic lesions. Plaques develop preferentially at arterial bifurcations, branch points, and regions exposed to disturbed or non laminar blood flow. In these areas, endothelial cells experience altered shear stress that impairs their physiological protective functions and enhances vascular permeability to circulating lipoproteins (Souilhol et al., 2020; Warboys & Weinberg, 2021; Kotlyarov, 2021). The resulting endothelial dysfunction facilitates leukocyte adhesion, inflammatory cell infiltration, and lipid retention, creating a local microenvironment that favors plaque initiation and progression.

Consequently, the interaction between lipid accumulation, vascular inflammation, and abnormal blood flow collectively determines the distribution and severity of atherosclerotic lesions. The clinical consequences of atherosclerosis are substantial because it serves as the primary pathological mechanism underlying ASCVD, including coronary artery disease, ischemic stroke, and peripheral artery disease. Plaque progression gradually compromises arterial blood flow, whereas plaque rupture or erosion can abruptly trigger thrombus formation and complete vascular occlusion. These acute thrombotic events frequently manifest as myocardial infarction or ischemic stroke and account for a considerable proportion of cardiovascular mortality worldwide. Epidemiological evidence indicates that approximately 75% of acute myocardial infarctions result from rupture of vulnerable atherosclerotic plaques, highlighting the importance of maintaining plaque stability in addition to reducing plaque burden.

The burden of cardiovascular disease attributable to atherosclerosis remains remarkably high. In the United States alone, approximately 610,000 individuals die from heart disease each year, representing nearly one quarter of all deaths. Coronary heart disease accounts for more than 370,000 deaths annually and continues to be the leading cause of mortality in many Western countries. Furthermore, an estimated 735,000 Americans experience myocardial infarction each year, including approximately 525,000 first time events and 210,000 recurrent episodes. These statistics illustrate the enormous healthcare burden associated with atherosclerosis and emphasize the urgent need for more effective preventive and therapeutic strategies aimed at reducing cardiovascular risk. The epidemiology of atherosclerosis also demonstrates important differences according to age and sex. Men generally develop clinically significant atherosclerotic disease earlier than women, with the highest incidence of plaque rupture occurring after the age of 45 years.

In contrast, women experience a marked increase in cardiovascular risk after the age of 50 years, particularly following menopause. This difference has largely been attributed to the protective effects of endogenous estrogen, which favorably influences lipid metabolism, endothelial function, oxidative stress, and vascular inflammation. However, the decline in estrogen levels after menopause diminishes these protective mechanisms, resulting in a rapid increase in the prevalence of atherosclerosis among older women (Davezac et al., 2021; Prabakaran et al., 2021; Somani et al., 2019). Although conventional management strategies,

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including lipid lowering therapy, antihypertensive treatment, antiplatelet agents, and lifestyle modification, have significantly reduced cardiovascular events, residual risk remains substantial in many patients. Clinical and experimental evidence suggests that persistent vascular inflammation continues to promote plaque progression even after optimal control of traditional cardiovascular risk factors. This observation has stimulated growing interest in therapeutic approaches that simultaneously target lipid metabolism and inflammatory pathways.

Advances in molecular biology have further identified several signaling pathways involved in vascular inflammation, offering new opportunities for the development of more targeted interventions capable of improving plaque stability and reducing cardiovascular complications. Given the central role of chronic inflammation in the initiation, progression, and destabilization of atherosclerotic plaques, understanding the underlying molecular mechanisms has become essential for developing innovative therapeutic strategies (Gusev & Sarapultsev, 2023; Raggi et al., 2018; Popa-Fotea et al., 2023). A comprehensive understanding of the interactions among lipid metabolism, endothelial dysfunction, immune activation, and inflammatory signaling will facilitate the identification of novel pharmacological targets for preventing plaque progression and reducing the incidence of ASCVD. Therefore, further investigation into the inflammatory mechanisms of atherosclerosis is expected to contribute significantly to the advancement of more effective preventive and therapeutic approaches aimed at reducing the global burden of cardiovascular disease.

METHODS

Research Sources and Methods

The purpose of this review is to determine the antioxidant properties and their role as Reactive Oxygen Species (ROS) scavengers in olive oil on the atherosclerosis process. A search was conducted using electronic databases such as PubMed, Scopus, Sinta, and Google Scholar. These electronic databases were assessed from 2020 to 2026. Additional studies were also identified by reviewing reference lists based on journal titles and individual keywords related to olive oil and atherosclerosis.

Keywords

"Olive" OR "Olea europea" AND antioxidant effect on atherosclerosis

"Olive oil" OR "Olea europea" AND atherosclerosis

Research Article Selection/Inclusion and Exclusion Criteria

The study was limited to research articles published between 2020 and 2026 in Indonesian and English. The inclusion criteria were as follows: (1) Full research articles; (2) Research reported in both Indonesian and English; (3) Research conducted between 2020 and 2026; (4) Research addressing individuals with atherosclerosis risk factors (hyperlipidemia, hypertension, diabetes, obesity); (5) Research determining the antioxidant effects of olive oil. The exclusion criteria for this study were: (1) Review articles, news articles, letters, editorials, and unpublished data such as theses; (2) Research utilizing a combination of plants and isolated compounds; (3) Duplicate research; and irrelevant titles. Studies meeting these criteria were excluded.

Data Extraction and Management

Articles were thoroughly screened before being selected for this systematic review. First, any paper that did not meet the inclusion criteria in the title was excluded. Second, article abstracts were screened and any articles that did not meet the inclusion criteria were excluded and duplicate studies were removed. Finally, the remaining articles were examined and any articles that did not meet the inclusion criteria were excluded. The data taken from the articles were as follows: (1) Title of the research article; (2) Research method; (3) Research results; (4) Research conclusion. This study used a systematic review method. Literature was obtained by reviewing scientific articles or journals downloaded from PubMed, NCBI (National Library of

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Medicine) and Google Scholar with minimum standards of SINTA V and Scopus Q5 as listed in Figure 1. Articles were screened based on the following provisions: articles published in 2020-2026, articles published that can be downloaded in full text and have open access, articles with qualitative and quantitative designs that discuss Olive Oil, antioxidants, polyphenols and atherosclerosis.

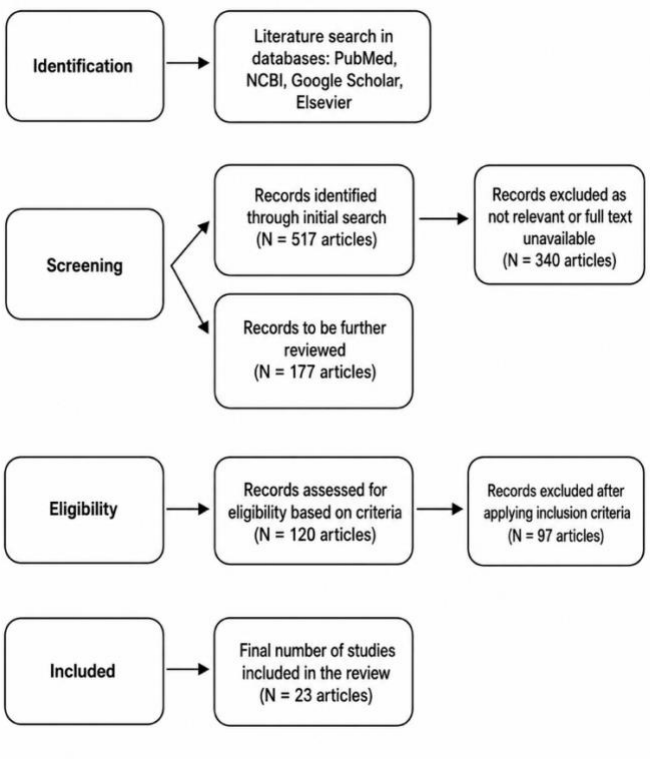

Figure 1. Flow Diagram of the Literature Search and Study Selection Process

RESULT AND DISCUSSION

As shown in the flowchart (Figure 1), approximately 517 articles were initially identified using keywords. After several screening processes based on inclusion and exclusion criteria, the articles selected for review and summary are presented in the table:

No.	Research Title	Objective	Research Methods	Results	Conclusion	Reference
1.	Mediterranean Diet Reduces Atherosclerosis Progression in Coronary Heart Disease	Analyzing the long-term effects of a Mediterranean diet compared to a low-fat diet on the progression of atherosclerosis in coronary heart disease patients.	A prospective, single-blind, randomized controlled trial (RCT), part of the CORDIOPREV study. 939 patients with coronary artery disease (CAD) were included. Interventions: Mediterranean diet (rich in extra virgin olive oil) vs. low-fat diet. Follow-up at 5 and 7 years. Outcomes: carotid intima-media	The Mediterranean diet significantly slowed the progression of atherosclerosis compared to a low-fat diet. There was improvement or a slowing of the increase in BMI-CC and carotid plaque parameters in the Mediterranean diet group, especially in patients at high metabolic risk.	Long-term consumption of a Mediterranean diet rich in extra virgin olive oil, compared with a low-fat diet, is associated with reduced atherosclerosis progression, as demonstrated by reduced BMI-CC and carotid plaque height. These findings reinforce the clinical benefits of the	Jimenez-Torres et al., 2021

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			thickness (IMT-CC), plaque count, and maximum plaque height by ultrasound.		Mediterranean diet in the context of secondary prevention of cardiovascular disease.	
2.	Effect of virgin olive oil as spreadable preparation on atherosclerosis compared to dairy butter in Apoe-deficient mice	To assess the role of olive oil and/or its bioactive components on oxidative stress, inflammation, and atherosclerosis progression..	Review of experimental and clinical scientific articles evaluating the effects of olive oil components (MUFA, polyphenols such as hydroxytyrosol and oleuropein) on biomarkers of oxidative stress, LDL oxidation, inflammation, and endothelial function.	Olive oil exhibits antioxidant effects by reducing ROS and oxidized LDL, increasing the activity of antioxidant enzymes (SOD, catalase), improving endothelial function, and reducing inflammatory mediators. The protective effect is stronger in polyphenol-rich extra virgin olive oil..	Consumption of olive oil, especially extra virgin olive oil, plays a role in preventing and slowing the development of atherosclerosis through antioxidant and anti-inflammatory mechanisms.	Martínez-Beamonte et al., 2024
3.	Effects of High-Phenolic Extra Virgin Olive Oil (EVOO) on the Lipid Profile of Patients with Hyperlipidemia: A Randomized Clinical Trial	To assess the effects of polyphenol-enriched extra virgin olive oil (EVOO) consumption on oxidative stress, endothelial function, and cardiovascular risk biomarkers in individuals at risk for cardiovascular disease..	Randomized controlled trial (double-blind, crossover design). Participants consumed EVOO with varying polyphenol concentrations for a specific intervention period, and then measured oxidative biomarkers, inflammation, lipid profiles, and vascular function.	Consumption of high-polyphenol EVOO significantly reduced oxidized LDL, increased plasma antioxidant capacity, improved endothelial function, and reduced inflammatory mediators compared to control or low-polyphenol EVOO.	Polyphenol-rich EVOO exerts protective effects against atherosclerosis through antioxidant and anti-inflammatory mechanisms, and has the potential to reduce the risk of cardiovascular disease in at-risk populations.	Kourek et al., 2025
4.	Biological Activities Underlying the Cardiovascular Benefits of Olive Oil Polyphenols: Focus on Antioxidant, Anti-Inflammatory, and Anti-Atherogenic Effects	To investigate the biological activities underlying the cardiovascular benefits of olive oil polyphenols, particularly their antioxidant, anti-inflammatory, and anti-atherogenic effects, and to compare	In vitro experimental study using J774 and THP-1 macrophages. ROS (DCFH-DA), lipid peroxidation (TBARS), inflammatory marker expression (CD86, CD163, IL-10, IL-6, IFN-α, IL-1β, NLRP3) were evaluated by flow cytometry, and cholesterol efflux (ABCA1-mediated)	EVOOPE+ exhibited stronger antioxidant activity at low concentrations (↓ ROS and lipid peroxidation). Both extracts decreased pro-inflammatory markers (CD86, IFN-α, NLRP3) and increased anti-inflammatory markers (CD163, IL-10). Furthermore, they increased cholesterol efflux in a dose-dependent	EVOO polyphenols have cardioprotective effects through antioxidant, anti-inflammatory, and reverse cholesterol transport mechanisms. Higher polyphenol content increases biological	Boumezough et al., 2025

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		standard EVOO and high-polyphenol EVOO..	assay. Compared with regular EVOO extract (EVOOPE), high-polyphenol EVOO (EVOOPE+), hydroxytyrosol (HT), and tyrosol (Tyr) extracts.	manner, with the strongest effects in EVOOPE+ and HT. A biphasic response pattern was observed (effects decreased at higher doses).	effectiveness, but optimal dosage is important due to the biphasic effects at high concentrations.	
5.	The intake of flavonoids, stilbenes, and tyrosols, mainly consumed through red wine and virgin olive oil, is associated with lower carotid and femoral subclinical atherosclerosis and coronary calcium	To assess the association between dietary polyphenol intake and subclinical atherosclerosis (carotid, femoral plaque, and coronary calcium scores) in middle-aged adult subjects without clinical cardiovascular disease..	A cross-sectional, cohort-based observational study (Aragon Workers' Health Study). Polyphenol intake was calculated using a food frequency questionnaire and a polyphenol database; atherosclerosis was assessed using carotid and femoral ultrasound and coronary artery calcium score (CACS). Analysis used logistic regression and linear regression with multivariate adjustment.	Intake of total polyphenols and some specific classes (especially flavonoids and stilbenes) was associated with lower plaque prevalence and coronary calcium scores after adjustment for confounding factors. There was a protective trend against subclinical atherosclerosis in individuals with higher polyphenol intake..	Higher dietary polyphenol intake is associated with a lower risk of subclinical atherosclerosis, supporting a protective role of polyphenol-rich diets in the prevention of cardiovascular disease.	Salazar et al. 2022
6.	Olive oil protects against cardiac hypertrophy in D-galactose induced aging rats.	Assessing the effect of olive oil consumption on oxidative stress and cardiovascular disease risk factors	An experimental study on male Wistar rats was conducted, divided into three groups: control, aging group induced by D-galactose (150 mg/kg intraperitoneally for 8 weeks), and treatment group (D-GAL + oral olive oil for 8 weeks). Oxidative stress, molecular parameters, and heart tissue histology were analyzed.	D-galactose administration caused cardiac hypertrophy (increased cardiomyocyte diameter), increased MDA, decreased SOD, and decreased gene expression of SIRT1, PGC-1α, TFAM, and Bcl2, as well as increased Bax. Olive oil administration improved all of these parameters: decreased hypertrophy and MDA, increased SOD, and improved gene expression related to mitochondrial function and apoptosis.	Olive oil exerts protective effects against D-galactose-induced cardiac aging through enhancing antioxidant effects and regulating the expression of SIRT1, PGC-1α, TFAM, and Bcl2, and Bax genes.	Sahidi et al., 2024

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7.	Chemical evaluation of arbequina extra virgin olive oil with in silico analysis of its key phenolic compounds targeting LDL metabolism	To evaluate the chemical characteristics of extra virgin olive oil (EVOO) of the Arbequina variety and to analyze in silico the potential of phenolic compounds (oleocanthal, oleacein, luteolin, tyrosol) on LDL metabolism compared to drugs (ezetimibe, bempedoic acid)	Experimental and computational studies (in vitro + in silico); GC-FID analysis (fatty acids), HPLC (phenolic compounds), spectrophotometry (TPC, PV, FFA, pigments); ADMET, DFT, molecular docking analysis on LDLR, PCSK9, ACLY targets	EVOO contains major phenolic compounds (oleacein, oleocanthal, luteolin, tyrosol); the compounds meet drug-likeness criteria; inhibit the OATP1B1/OATP1B3 transporter and CYP enzymes; molecular docking shows that oleacein has the best affinity for LDLR, while luteolin has the best affinity for PCSK9 and ACLY.	EVOO phenolic compounds (especially oleacein, oleocanthal, luteolin) have potential as therapeutic agents in the regulation of LDL metabolism and atherosclerosis, but further in vitro and clinical research is still needed.	Korkmaz et al., 2025
8.	Extra Virgin Olive Oil (EVOO) Improves Vascular Endothelial Function and Hemodynamic Parameters in Patients with Hyperlipidemia: A Post Hoc Analysis of a Randomized Controlled Trial	MExtra virgin olive oil (EVOO) exhibits potent antioxidant and anti-inflammatory properties. Recent findings from our Institute indicate that its bioactive compounds improve lipid metabolism, suggesting EVOO as a promising nutritional intervention for hyperlipidemia patients. This clinical study aimed to evaluate the effects of EVOO consumption on vascular endothelial function and hemodynamic parameters in hyperlipidemic	This post-hoc analysis included 70 participants: 50 patients with hyperlipidemia and 20 healthy controls. All participants consumed EVOO daily for four weeks. Hyperlipidemia patients were randomized into two subgroups: one receiving high-phenolic EVOO at a low dose and the other receiving low-phenolic EVOO at a high dose, ensuring equivalent total polyphenol intake. Vascular endothelial function, assessed by near-infrared spectroscopy (NIRS), served as the primary endpoint, while arterial blood pressure and heart rate were	Hyperlipidemic patients showed significant improvements in endothelial function, with increased reperfusion rates ($p = 0.010$) and oxygen consumption rates ($p < 0.001$) compared to controls. Reductions in the time to maximum hyperemia ($p = 0.004$) and hyperemia recovery time ($p < 0.05$) further indicated improved vascular function. Diastolic blood pressure ($p = 0.007$) and heart rate ($p = 0.004$) decreased significantly. Among the subgroups, high-phenolic EVOO at lower doses was more effective in reducing systolic blood pressure ($p = 0.049$) and increasing	EVOO consumption improves endothelial function and hemodynamic parameters in hyperlipidemic patients, with high-phenolic EVOO showing superior vascular benefits at lower doses.	Kourek et al., 2025

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		individuals, while comparing two types of EVOO that differ in polyphenol content and dosage.	secondary endpoints. Statistical analysis used a linear mixed model.	reperfusion rates (p = 0.049).		
9.	Effect of Extra Virgin Olive Oil High in Bio active Compounds on Atherosclerosis in Apoe-Deficient Mice	To assess the effects of extra virgin olive oil (EVOO) enriched with bioactive compounds (EVOO HBC) on the development of atherosclerosis and fatty liver in ApoE-deficient mice.	In vivo experimental study in ApoE-deficient mice for 12 weeks with three isocaloric diets (palm fat, EVOO, EVOO HBC); plasma lipid analysis, lipoprotein characterization, CD36 monocyte expression, M2 macrophage, liver squalene levels, and atherosclerotic lesions (en face and cross-sectional) were performed.	The EVOO group showed increased triglycerides and glucose without changes in total cholesterol; decreased lipoprotein oxidation; decreased CD36 expression; increased M2 macrophages; hepatic squalene accumulation; and decreased atherosclerotic lesions compared to palm oil; there were differences in response between males and females.	EVOO, especially those enriched in bioactive compounds (high in squalene and oleuropein aglycone), may reduce the development of atherosclerosis through modulation of inflammation, lipoprotein function, and macrophage activity, with effects influenced by gender.	Martínez-Beamonte et al., 2025
10.	The Immunomodulatory Effects of a 6-Month Extra Virgin Olive Oil Intervention on Monocyte Cytokine Secretion and Plasma Cytokine Levels in Dyslipidemic and Post-Infarct Patients: A Clinical Pilot Study	Assessing the nutraceutical potential of extra virgin olive oil (EVOO) on monocyte inflammatory status in individuals with varying levels of cardiovascular risk.	An intervention study of 43 participants aged 65–85 years (healthy, dyslipidemic, and post-infarction) who were given 25 mL/day of EVOO supplementation for 6 months; cytokine production (IL-1β, IL-6, IL-10, TNF-α) and monocyte phenotype were analyzed using flow cytometry under basal and stimulated conditions.	At the beginning of the study, dyslipidemia patients showed an inflammatory state with lower IL-10 production; after 6 months of intervention, there were no significant changes in monocyte phenotype or IL-10, IL-6, and TNF-α production; there was an increase in IL-1β in post-infarction patients; in dyslipidemia patients there was a decrease in IL-1β secretion upon stimulation despite an increase in basal conditions.	EVOO intervention for 6 months did not provide significant changes in monocyte phenotype or cytokine production, so the anti-inflammatory effect on monocytes was not significantly proven in this study.	Zimmer et al., 2023

Atherosclerosis is a chronic inflammatory disease characterized by the buildup of plaque within the arteries. This plaque is primarily composed of lipids, which trigger an inflammatory reaction and cause turbulent flow, resulting in atherosclerotic cardiovascular disease.

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Atherosclerosis develops through a continuous process of arterial wall lesions caused by lipid retention with intimal entrapment by a matrix such as proteoglycans. This modification, in turn, exacerbates chronic inflammation at vulnerable points in the artery and plays a key role in all phases of atherogenic development. This process begins with a newly formed fatty layer in the arterial intima, which then develops into a fibrous plaque and emerges as a complex atherosclerotic lesion susceptible to rupture. Furthermore, stenosis due to inward expansion of atheroma can lead to occlusion of blood vessels such as the coronary arteries. The systemic changes detected in atherosclerosis are very similar in the aorta, coronary arteries, and carotid arteries.

The process of LDL oxidation to oxidized LDL (ox-LDL) plays a key role in initiating and accelerating atherosclerotic plaque formation through inflammatory response activation, endothelial dysfunction, and foam cell formation. In this context, oxidative stress is a key factor that not only acts as an initial trigger but also accelerates the progression of atherosclerosis through increased production of Reactive Oxygen Species (ROS) and biomolecular damage (Ajoolabady et al., 2024).

Based on the results of various studies reviewed in this systematic review, olive oil, particularly extra virgin olive oil (EVOO), exhibits a significant protective effect against oxidative stress and the development of atherosclerosis. This effect is primarily due to its bioactive compounds, such as oleic acid and polyphenols (hydroxytyrosol, tyrosol, oleuropein, oleocanthal, and oleacein), which possess potent antioxidant activity. These compounds work by neutralizing free radicals, inhibiting lipid peroxidation, and protecting LDL from oxidation, thereby reducing the formation of ox-LDL (Korkmaz et al., 2025).

Experimental and clinical studies have shown that olive oil consumption is associated with reduced oxidative stress biomarkers such as malondialdehyde (MDA) and ox-LDL, as well as increased activity of antioxidant enzymes such as superoxide dismutase (SOD). A study by Shahidi et al. (2024) showed that administering olive oil to an animal model reduced MDA levels and increased SOD, indicating improved oxidative balance (Ajoolabady et al., 2024).

Furthermore, the polyphenol content in EVOO has a stronger effect in inhibiting oxidative stress. In vitro studies have shown that EVOO with a high polyphenol content significantly reduces ROS production and lipid peroxidation and increases cellular antioxidant capacity (Boumezough et al., 2025). Clinical studies have also shown that EVOO high in polyphenols can reduce oxidized LDL and improve endothelial function compared to standard EVOO. In addition to its antioxidant effects, olive oil also plays a role in inhibiting inflammation, which is closely related to oxidative stress (Bucciantini et al., 2021; Santangelo et al., 2018; Luisi et al., 2019; Summerhill et al., 2018; Casas et al., 2018; Lama et al., 2017). Polyphenols in olive oil are known to inhibit the activation of inflammatory pathways such as NF-κB and reduce the production of pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α. Research has shown that phenolic compounds in olive oil can increase anti-inflammatory markers such as IL-10 and enhance reverse cholesterol transport by increasing cholesterol efflux (Boumezough et al., 2025).

Olive oil also contributes to improving endothelial function and lipid metabolism. Clinical studies have shown that EVOO consumption can improve vascular endothelial function, improve hemodynamic parameters, and lower blood pressure in patients with hyperlipidemia. Furthermore, the phenolic compounds in olive oil also have the potential to regulate LDL metabolism through interactions with the LDL receptor (LDLR) and the PCSK9 protein, thus contributing to lower circulating LDL levels (Korkmaz et al., 2025).

However, not all studies have shown consistent results. A study by Zimmer et al. (2023) reported that a 6-month EVOO intervention did not significantly alter inflammatory cytokine production in monocytes, although there was a trend toward improvement in several inflammatory parameters. This suggests that the effects of olive oil may be influenced by factors such as dose, duration of intervention, and the condition of the study subjects (Gonzalez et al., 2023).

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The Role of Extra Virgin Olive Oil in Endothelial Function

The bioactive compounds in extra virgin olive oil (EVOO), particularly polyphenolic compounds such as hydroxytyrosol, oleocanthal, and oleacein, play a crucial role in improving endothelial function impaired by atherosclerosis. Endothelial dysfunction is an early stage in the pathogenesis of atherosclerosis, characterized by decreased nitric oxide (NO) bioavailability, increased oxidative stress, and the activation of adhesion molecules such as VCAM-1 and ICAM-1. Clinical studies have shown that EVOO consumption significantly improves vascular endothelial function by increasing tissue perfusion and lowering blood pressure, particularly in individuals with hyperlipidemia. This mechanism is mediated by the ability of EVOO polyphenols to reduce the production of reactive oxygen species (ROS), inhibit the activation of inflammatory pathways such as NF-κB, and increase the activity of endothelial nitric oxide synthase (eNOS), which plays a role in NO production. Furthermore, EVOO's phenolic compounds also play a role in inhibiting LDL oxidation, thereby reducing the formation of ox-LDL, which is toxic to endothelial cells. Thus, EVOO not only functions as an antioxidant but also as a protective agent capable of repairing endothelial dysfunction and slowing the progression of atherosclerosis (Korkmaz et al., 2025; Gonzalez et al., 2023).

Mechanism of Action

The bioactive compounds in extra virgin olive oil (EVOO), particularly polyphenolic compounds such as hydroxytyrosol, tyrosol, oleuropein, and oleocanthal, play an important role in inhibiting oxidative stress in cardiovascular disease through various molecular mechanisms, namely: (1) The ability of polyphenols to neutralize reactive oxygen species (ROS), thereby preventing oxidative damage to lipids, proteins, and DNA; (2) EVOO polyphenols can activate endogenous antioxidant pathways through the activation of nuclear factor erythroid 2-related factor 2 (Nrf2), which increases the expression of antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase; (3) Another important mechanism is the inhibition of lipid peroxidation, specifically preventing the oxidation of low-density lipoprotein (LDL) to oxidized LDL (ox-LDL), which is a major factor in the pathogenesis of atherosclerosis; (4) The phenolic compounds in EVOO can also inhibit the activation of inflammatory pathways such as nuclear factor-kappa B (NF-κB), thereby reducing the production of pro-inflammatory cytokines that contribute to vascular damage; (5) The oleic acid content in EVOO also plays a role in increasing cell membrane stability and reducing lipid oxidation. Overall, EVOO's mechanism of action against oxidative stress involves a complex interaction between direct antioxidant activity, enhancement of the endogenous antioxidant defense system, and modulation of inflammatory pathways and lipid metabolism, thus providing a protective effect against the development of cardiovascular disease (Milena & Maurizio, 2025; Serreli et al., 2024).

Benefits of Olive Oil Against Cardiovascular Disease

The main components of EVOO, such as oleic acid and polyphenolic compounds (hydroxytyrosol, oleuropein, and oleocanthal), act as powerful antioxidants and anti-inflammatories. EVOO polyphenols have been shown to protect blood lipids from oxidative damage by inhibiting low-density lipoprotein (LDL) oxidation, thus preventing the formation of oxidized LDL (ox-LDL), a major factor in the pathogenesis of atherosclerosis. Furthermore, EVOO improves endothelial function, lowers blood pressure, and improves lipid profiles by lowering LDL levels and increasing high-density lipoprotein (HDL) levels. This mechanism is enhanced through the activation of antioxidant pathways such as nuclear factor erythroid 2-related factor 2 (Nrf2) and inhibition of the nuclear factor-kappa B (NF-κB) inflammatory pathway, which contribute to reducing oxidative stress and vascular inflammation. Epidemiologically, regular olive oil consumption is also associated with a reduced risk of cardiovascular disease and mortality. Thus, EVOO can be categorized as an effective nutritional intervention in the prevention and management of cardiovascular disease (Milena & Maurizio, 2025).

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CONCLUSION

Oxidative stress plays a key role in the initiation and progression of atherosclerosis through increased production of reactive oxygen species (ROS), which cause biomolecular damage and endothelial dysfunction. Olive oil, particularly extra virgin olive oil (EVOO), has been shown to have a protective effect against the development of atherosclerosis through its bioactive components, particularly oleic acid and polyphenolic compounds such as hydroxytyrosol, oleuropein, oleocanthal, and oleacein. These compounds act as antioxidants that neutralize ROS, inhibit lipid peroxidation, and prevent the oxidation of LDL to oxidized LDL (ox-LDL), thereby reducing the formation of atherosclerotic plaque. Furthermore, EVOO enhances the endogenous antioxidant defense system through activation of the Nrf2 pathway and suppresses the inflammatory response through inhibition of the NF-κb pathway. The mechanism of action of EVOO in suppressing oxidative stress involves multi-target interactions, namely direct antioxidant activity, increased antioxidant enzymes, inhibition of inflammation, and regulation of lipid metabolism. Although some studies have shown inconsistent results, overall, the scientific evidence suggests that EVOO has significant benefits in preventing and slowing the progression of cardiovascular disease. Therefore, extra virgin olive oil consumption can be considered an effective nutritional intervention in the prevention and management of atherosclerosis through mechanisms such as reducing oxidative stress, improving endothelial function, and modulating inflammation and lipid metabolism.

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