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Article Review

The Effectiveness of Olive Oil in Preventing Atherosclerosis: A Literature Review

Rachmat Faisal Syamsu[1*], Yugni Maula Thahira[2], Hermiaty Nasruddin[1], Dahlia[1], Rezky Putri Indarwati[1], Salahuddin Andi Palloge[1], Abbas Zavey Nurdin[1], Armanto Makmun[1], Burhanuddin Bahar[1]

[1]Department of IKM-IKK, Faculty of Medicine, Universitas Muslim Indonesia, Makassar, Indonesia
[2]Physician Professional Study Programme, Faculty of Medicine, Universitas Muslim Indonesia, Makassar, Indonesia

(Correspondence author's email, rachmatfaisal.syamsu@umi.ac.id)

ABSTRACT

Olive oil is a rich source of oleic acid and polyphenols. Extra virgin olive oil is rich in phenolic compounds which are known to have anti-inflammatory, anti-cancer, and antioxidant effects. Olive oil has been used for thousands of years as a food source and is reported to have beneficial effects on cardiovascular disease. This review aims to provide a comprehensive overview of the current literature on the use of olive oil in the prevention and treatment of cardiovascular diseases and prevention of atherosclerosis. The methodology is employed by searching the article at Google Scholar, PubMed, Semantic Scholar, teaching materials, and research gate. Studies included the consumption of olive oil, by using qualitative and quantitative methodologies, were published in journals between 2013 and 2024 to obtain the latest information and relevant contents of the articles as well as the empirical data that indicate the effectiveness of olive oil. This research has a varying result, such as the high level of cholesterol and low-density lipoprotein cholesterol (LDL-C). Olive oil polyphenols also increase HDL particle size increase HDL stability by producing a triglyceride-poor core, and improve HDL antioxidant status by increasing the olive oil polyphenol metabolite content of lipoproteins, and it can intake of several foods also positively modulates platelet reactivity and may be the basis for the reduced cardiovascular risk reported in individuals on diets that increase the intake of plant foods, such as the Mediterranean diet. The olive oil which contains MUFA in the form of oleic acid and polyphenols has anti-atherogenic properties to prevent cardiovascular disease.

Keywords: *Olive Oil, Atherosclerosis, Antioxidant.*

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INTRODUCTION

According to the World Health Organization (WHO) and the World Heart Federation, heart disease is currently the main cause of death in Asian and European countries. Every year an estimated 17.3 million people die from cardiovascular disease. As many as 11.1 million of them occurred due to heart disease and 6.2 million due to stroke. Heart disease and stroke occur due to blockage and hardening of the arteries called atherosclerosis[1].

Atherosclerosis is described as the "stiffening of the arteries" and is a chronic inflammatory process whose pathophysiology involves lipids, thrombosis, vascular walls, and immune cells[2].

This atherosclerosis process begins to form at a very early age, even while still in the mother's womb. In line with increasing age, and with the presence of risk factors, the process will further develop and give rise to diseases related to atherosclerosis and its complications. Atherosclerosis is a chronic inflammatory

process whose pathophysiology involves inflammation, lipids, thrombosis, and vascular walls including dysfunction of the endothelium and immune cells. The vascular endothelium will regulate vascular homeostasis by producing substances that can cause clotting or anti-clotting. The presence of inflammatory factors and other risk factors will cause the loss of the endothelial protective effect, including hyperlipidemia, hypertension, diabetes and smoking[2].

The Mediterranean diet is considered one of the mainstream diets and has long been known as one of the most effective ways to prevent and improve cardiovascular disease[3,4].

Olive oil is a typical fat source in the Mediterranean diet that has been shown to have important nutritional value and a positive impact on human health due to its bioactive composition[4,5]. The main component of olive oil which is associated with its anti-atherogenic properties in preventing cardiovascular disease is the MUFA oleic acid which makes up 55-83% of the total fatty acids and minor components of olive oil such as phenolic compounds which amount to 1-2% of the total olive oil content[4,6].

The high MUFA content in olive oil significantly reduces the concentration of total cholesterol (TC) and LDL cholesterol (LDL-C), reducing the TC/HDL and LDL/HDL ratios. Phenolic compounds, especially hydroxytyrosol and oleuropein, inhibit the oxidation of LDL and HDL in vitro and in vivo, inhibit superoxide-induced reactions, and interrupt the propagation of lipid peroxides.(6) Consumption of foods rich in polyphenols has also been shown to increase the bioavailability of nitric oxide (NO) as well as reduce oxidative stress and inflammation.[7].

EVOO's high nutritional value lies largely in its rich and complex chemical profile containing more than 200 compounds. MUFA in the form of oleic acid (OA) is the main component of EVOO which contributes up to 70%–80%. Other minor but nutritious components, such as phenolic compounds, squalene and tocopherol, account for approximately 1%–2% of EVOO content. Although these minor components (such as chlorophyll and carotenoids) also contribute to the beneficial effects of EVOO, the pharmacological effects of EVOO are mainly due to its main components, OA and polyphenols[4].

This review aims to provide a comprehensive overview of the current literature on the use of olive oil in the prevention and treatment of cardiovascular diseases and prevention of atherosclerosis.

METHOD

A literature search was conduct using the following electronic database such a, Google scholar, PubMed, semantic scholar, teaching materials, research gate to identify the research publications. In addition, we manually search the cited of data and review article for many pertinent studies.

Studies were included the consumption of olive oil, by using qualitative and quantitative methodologies, were published in journal between 2013 and 2024 to obtain the latest information and relevant contents of the articles as well as the empirical data which indicate the effectiveness of olive oil. Each article have a different sources and methodologies to find out the result of the research.

RESULTS AND DISCUSSION

Marta et al conducted a prospective cohort study followed for 24 years, finding an inverse association between olive oil consumption and cardiovascular events. Compared with non-consumers, people who consumed more olive oil had a 14% lower risk of cardiovascular disease and an 18% lower risk of coronary heart disease. In addition, it is estimated that compared with margarine, butter, mayonnaise, and milk fat, olive oil is associated with a lower risk of cardiovascular disease (CVD) and CHD, whereas when compared with other vegetable oils combined, olive oil is not associated with CVD. This research produces new evidence showing that replacing saturated fats, such as butter and margarine, with healthy vegetable fats, such as olive oil, is beneficial for the primary prevention of CVD. Additionally, higher olive oil intake was associated with lower levels of inflammatory biomarkers and better lipid profiles, suggesting that moderate olive oil intake may provide some benefit on surrogate markers of CVD[13].

Evaluation of the thickness of the intima-media layer of both common carotid arteries or intima-media thickness of both common carotid arteries (IMT-CC) using B-

mode ultrasound is a noninvasive and well-validated clinical method as a surrogate marker of subclinical atherosclerosis and a strong predictor of infarction. new myocardium and stroke. Jose et al's study evaluated the efficacy of two healthy diet patterns (a Mediterranean diet rich in EVOO compared with a diet low in fat and rich in complex carbohydrates) in reducing IMT-CC in patients with coronary heart disease. The Mediterranean diet reduced IMT-CC at 5 years (−0.027±0.008 mm; P<0.001), maintained at 7 years (−0.031±0.008 mm; P<0.001), compared with baseline values. A low-fat diet did not change BMI-CC. IMT-CC and carotid plaque height decreased more after the Mediterranean diet, compared with the low-fat diet during the follow-up period[14].

High levels of total cholesterol and low-density lipoprotein cholesterol (LDL-C) are known risk markers for atherosclerosis. It is considered a major cause of CVD while high-density lipoprotein cholesterol (HDL-C) is thought to be protective[15]. Several epidemiological and interventional studies have shown that there is an inverse relationship between plasma HDL levels and CVD[16].

Oxidation of low-density lipoprotein (LDL) is an early event in the development of atherosclerosis, the main cause of CHD. Oxidized LDL is not recognized by the LDL receptor Apo (B/E) but is taken up by macrophages in an unregulated manner via the scavenger-receptor pathway, leading to the formation of foam cells, a characteristic feature of arteriosclerotic lesions. Macrophage-specific reverse cholesterol transport (RCT) is considered one of the most important HDL-mediated cardioprotective mechanisms. RCT is the process by which cholesterol in peripheral cells is removed to circulating HDL and transported back to the liver for excretion in bile and feces. RCT is considered the main antiatherogenic function of HDL. Two major macrophage cholesterol efflux pathways have been described: SR-BI receptor-mediated cholesterol efflux and ABCA1/ABCG1-mediated cholesterol efflux. ABCA1 promotes the efflux of phospholipids and cholesterol to lipid-poor apo-AI through a process involving direct binding of apo-AI to the ABCA1 transporter, whereas ABCG1 and SR-BI are the main mediators of macrophage cholesterol efflux to HDL[6].

The results of Hicham et al's research showed an increase in LDL and HDL resistance to lipid peroxidation. This effect may be due to the antioxidant effect of phenolic compounds that can capture reactive oxygen species and thereby inhibit lipoprotein oxidation. Olive oil polyphenols also increase HDL particle size, increase HDL stability by producing a triglyceride-poor core, and improve HDL antioxidant status by increasing the olive oil polyphenol metabolite content of lipoproteins. Thus, EVOO enhances the anti-atherogenic properties of HDL by reducing oxidative modifications and by maintaining the physicochemical properties of HDL, which in turn improves HDL function, especially the capacity to increase cholesterol efflux. EVOO also protects cells from oxidative damage and stimulates the expression of the ABCA1 protein, a key factor in cholesterol efflux and HDL formation[6].

The results of clinical trials in healthy people as well as individuals at high cardiovascular risk, who followed a traditional Mediterranean diet supplemented with virgin olive oil for a long period showed that olive oil can induce the resistance of HDL to oxidation, and therefore, maintain its vasodilatory capacity (HDL can induces the release of nitric oxide in endothelial cells by activating eNOS). In addition, human studies indicate that phenolic compounds can protect LDL from oxidation, as demonstrated by reducing the oxidizing ability of LDL and modulating the oxidative effects of LDL ox. Polyphenol-rich olive oil has also been shown to reduce the concentration and atherogenicity of circulating LDL[17].

Lipid profiles improved in participants in the EUROLIVE human crossover study, in which 200 European participants consumed olive oil for three weeks. Participants were randomly divided into three groups of olive oils that differed in phenolic content (low, medium and high). HDL-C increased linearly with phenolic content, whereas the TC/HDL-C ratio decreased linearly. The LDL-C/HDL-C ratio and triglycerides decreased in those consuming medium and high phenolic olive oil. Smaller trials in humans confirmed that phenol-rich olive oil improved the lipid profile in terms of circulating HDL-C, lowering LDL-C and to a greater but lesser extent triacylglycerol-rich lipoproteins (TRL)[15].

Research from Katerina et al showed that a non-significant average increase in serum HDL cholesterol efflux capacity was observed in the extra virgin low polyphenol (LPOO) and

high polyphenol (HPOO) treatment groups after consuming both types of OO for 3 weeks respectively. Additionally, significant increases in circulating HDL cholesterol were observed in both treatment groups[18].

The first anti-inflammatory mechanism attributed to olive oil is the ability of the main phenolic compounds to inhibit the adhesion of immune cells (T, B lymphocytes and monocytes) to the endothelium, in response to the inflammatory process. This is achieved by inhibiting the expression of inflammatory mediators, such as cytokines (interleukin (IL)-1, IL-6, IL-8 and tumor necrosis factor-alpha (TNF-a) signaling pathways), chemokines (monocyte chemotactic protein (MCP-1) , adhesion molecules (P and E-selectin, intercellular adhesion molecule-1 (ICAM-1), and leukocyte adhesion molecules, namely vascular cell adhesion molecule-1 (VCAM-1), which are very important in the regulation of innate and adaptive immunoinflammatory responses. A recent study showed that hydroxytyrosol and its metabolites were protective against endothelial dysfunction in human aortic endothelial cells in combination with TNF-a by reducing the secretion of E-selectin, P-selectin, ICAM-1, and VCAM-1. hydroxytyrosol metabolites further reduced MCP-1 levels[17].

Platelets are the first response to vascular injury in the early stages of endothelial disruption, after plaque rupture, and in the late manifestations of disease; at the same time, it promote inflammatory processes that exacerbate atherosclerotic disease. Intake of several foods also positively modulates platelet reactivity and may be the basis for the reduced cardiovascular risk reported in individuals on diets that increase the intake of plant foods, such as the Mediterranean diet. What is interesting about the current trial is the effect of olive oil on platelet function[19].

Blood platelets have been shown to play a role in the development of atherosclerosis. The development of CHD has been associated with high levels of plasma coagulation factors and fibrinolytics such as plasminogen activator inhibitor-1 (PAI-1) and factor VII (FVII). Pure olive oil with a high content of phenolic compounds (400 mg/kg) has been shown to inhibit PAI-1 and FVII [15]. VOO exhibits anti-atherogenic effects, especially PL which acts as a Platelet-Activating Factor (PAF) inhibitor, tyrosol and oleuropein and αT which also exert anti-PAF activity[20].

Research from Ruina et al states that more frequent olive oil intake is associated with reduced thrombin-induced platelet activation in people with obesity. Platelet activation is measured by surface markers such as P-selectin. P-selectin is translocated to the platelet surface during activation and mediates platelet interactions with endothelial cells and immune cells. As a direct marker of platelet activation, P-selectin is increased in obesity and is positively associated with carotid intima medial thickness and the development of atherosclerosis and other vascular risk factors. Therefore, increased P-selectin is thought to contribute to the increased risk of CVD in obesity. Thrombin-induced platelet P-selectin expression is increased in severe obesity and normalizes after bariatric surgery[21].

Thrombin is a potent platelet agonist via proteinase-activated receptors (PAR). Activation of PAR in human platelets increases intracellular calcium, which in turn causes a signaling cascade and translocation of P-selectin from α-granules to the platelet surface. However, olive oil intake did not affect basal P-selectin expression in circulating platelets, affecting only thrombin-induced P-selectin. Polyphenols can block receptor-agonist interactions, such as PAR1-thrombin binding, leading to inhibition of downstream activation signals, reduced degranulation, and suppressed P-selectin translocation to the platelet surface[21].

A recent observational study showed that obese patients who frequently consumed OO (>4 times/week) showed lower thrombin-induced P-selectin expression on platelet counts compared with less frequent consumers (<1 time/week). This study clearly shows that increased OO consumption correlates with lower platelet activation however the type of OO consumed by the study volunteers was not identified[22].

CONCLUSIONS

Based on a review of some articles since 2013-2023, the researcher concluded that the olive oil which contains MUFA in the form of oleic acid and polyphenols, has anti-atherogenic properties to prevent cardiovascular disease such as congenital heart disease (CHD), high density lipoprotein (HDL).

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