



June, 2025 Popular Article



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Citation: Venkat et al., 2025. Squalene from Fish: The Natural Shield Against Heart Disease. Chronicle of Bioresource Management 9(2), 049-052.

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Data Availability Statement: Legal restrictions are imposed on the public sharing of raw data. However, authors have full right to transfer or share the data in raw form upon request subject to either meeting the conditions of the original consents and the original research study. Further, access of data needs to meet whether the user complies with the ethical and legal obligations as data controllers to allow for secondary use of the data outside of the original study.

Conflict of interests: The authors have declared that no conflict of interest exists.

Keywords:

Squalene, cardiovascular diseases, oxidative stress, anti-inflammatory

Article History

Article ID: CBM6203 Received on 06th March 2025 Received in revised form on 03rd May 2025 Accepted in final form on 15th May 2025

Squalene from Fish: The Natural Shield Against Heart Disease

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Abstract

Squalene, a naturally occurring triterpene, has gained significant attention for its potential cardiovascular protective effects, particularly when derived from fish sources. Fish-derived squalene, especially from deep-sea fish such as sharks and certain species of tuna and sardines, is rich in bioactive compounds that contribute to its therapeutic properties. This article explores the mechanisms through which squalene exerts cardioprotective effects, including its antioxidant activity, cholesterol regulation, anti-inflammatory properties, and ability to improve blood circulation and lower blood pressure. Scientific studies have demonstrated that squalene supplementation can reduce levels of LDL cholesterol and triglycerides, enhance HDL cholesterol, and decrease oxidative stress, all of which are key factors in preventing cardiovascular diseases (CVDs). Despite its potential, careful consideration of potential side effects, such as allergies or gastrointestinal discomfort, is necessary. Overall, fish-derived squalene presents a promising natural supplement for cardiovascular health, offering a safe and effective means of reducing CVD risk.

1. Introduction

One of the current serious health concerns is cardiovascular diseases, around the world every year 16.7 million people die due to myocardial infraction which is almost equal to one third of the total world deaths. It is anticipated that the leading cause for the death disability is due to the heart disease and stroke. So, in recent times cardiovascular disease research has grown to be a field of great importance. Thus, there is an urge for clinical development of safe cytoprotective agents for better management of cardiovascular diseases and health. As the oxidative stress is the major cause for many disorders like age related, cancer, cardiovascular diseases. So mitigation of oxidative stress is the better strategy to prevent the cardiovascular and other related diseases. Squalene is a naturally occurring triterpene compound that plays a critical role in the synthesis of sterols, including cholesterol, hormones, and vitamins. The structural formula of squalene was clarified in 1936 by Swiss chemist Paul Karrer, who worked at Zurich University, Switzerland. It is known structurally as (all-E) 2,6,10,15,19,23-hexamethyl-

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2,6,10,14,18,22-tetracosahexaene (Figure 1). Considering the functions squalene plays in the human body, it is appropriately called a "gift from the sea" (Sumi et al., 2018). It is found in a variety of sources, including plant oils, animal fats, and some marine organisms, with fish-derived squalene being one of the most significant sources for human health. Among its many biological functions, squalene has been recognized for its potential cardiovascular protective effects. This article explores the role of fish-derived squalene as a cardio-protector, examining its mechanisms of action, health benefits, and the scientific evidence supporting its use in cardiovascular health.

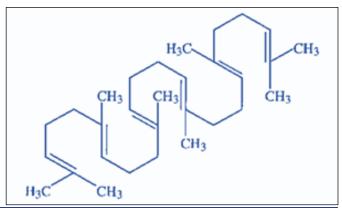


Figure 1: Chemical Structure of Squalene (Sumi et al., 2018)

2. Sources of Fish-Derived Squalene

Fish, particularly certain species of deep-sea fish, are rich sources of squalene, notably from their liver oils. These oils, extracted from species such as the deep-sea shark and certain fishlike mackerel and sardines, contain concentrations of squalene ranging from 5% to 10% by weight. In tropical deep-sea shark (*Centrophorus atromarginatus*) as much as 80% of its liver oil is squalene. basking shark liver oil also contains large quantities of squalene. Squalene from fish oils is considered to be of high quality due to its natural composition and favourable fatty acid profile, making it an important nutritional supplement for cardiovascular health (Figure 2).

3. Mechanisms of Action in Cardiovascular Protection

The potential cardiovascular protective effects of squalene can be attributed to its multifaceted biological activities (Figure 2). Several mechanisms have been identified through which squalene exerts a cardio-protective effect:

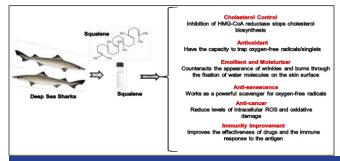


Figure 2: Fish-derived Squalene and its health benefits

3.1. Antioxidative effect

Squalene is a potent antioxidant, which helps reduce oxidative stress in the body. Oxidative stress plays a major role in the development of cardiovascular diseases (CVDs) by contributing to endothelial dysfunction, atherosclerosis, and inflammation. As an antioxidant, squalene can neutralize free radicals, protecting lipids, proteins, and DNA from oxidative damage, which in turn supports vascular health and reduces the risk of developing heart disease. Additionally, it also lowered levels of harmful enzymes (ALT, AST, LDH, CPK) and lipid peroxides, while increasing the activity of important antioxidant enzymes like GPx, GST, CAT, and SOD in the rats. These results suggest that squalene may help protect the heart by reducing oxidative damage and improving lipid profiles (Farvin et al., 2004).

Squalene strengthened the heart's cell membranes by reducing the release of harmful enzymes and counteracting free radicals. It also helped preserve antioxidants like ascorbic acid, tocopherol, and reduced glutathione. This antioxidant effect also inhibited lipid peroxidation and supported the heart tissue's structure.

3.2. Regulation of cholesterol

One of the key roles of squalene in cardiovascular health is its involvement in cholesterol metabolism (Ibrahim et al., 2020). Squalene is a precursor in the biosynthesis of cholesterol, and studies have shown that it may influence cholesterol levels in the body. In animal studies, squalene supplementation has been found to reduce total cholesterol levels, LDL cholesterol, and triglycerides while increasing HDL cholesterol, which is often referred to as "good cholesterol". These changes in lipid profiles contribute to a reduced risk of atherosclerosis and other cardiovascular conditions. Squalene reduced the increase in cholesterol, triglycerides, and free fatty acids in the blood and heart tissue. Hypercholesterolemia is a well-known risk factor for cardiovascular diseases. Plant-based products from the terpenoid family, such as squalene

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found in vegetable oils rich in mono- and polyunsaturated fatty acids, have been shown to reduce cholesterol levels in animal studies. Epidemiological research indicates that consuming squalene-rich olive oil is associated with a lower incidence of coronary heart disease. The cholesterol-lowering effect of squalene is attributed to its ability to inhibit HMG CoA reductase, an enzyme critical for cholesterol production.

3.3. Anti-inflammatory effect

Inflammation is a critical component of atherosclerosis and many other cardiovascular diseases. Squalene exhibits significant anti-inflammatory properties by modulating the production of pro-inflammatory cytokines and inhibiting the activation of inflammatory pathways such as NF-kB. By reducing chronic inflammation, squalene may prevent or slow the progression of cardiovascular diseases, including coronary artery disease and hypertension (Ibrahim and Naina Mohamed, 2021)

3.4. Improvement of endothelial cell function

The endothelium, the thin layer of cells lining blood vessels, is a key player in cardiovascular health. Dysfunction in endothelial cells can lead to the development of atherosclerosis, hypertension, and heart failure. Studies have shown that squalene can improve endothelial function by promoting nitric oxide production, which helps in vasodilation and improved blood flow.

3.5. Reduction in hypertension

Leptin is linked to cardiovascular problems associated with obesity and hypertension, as many obese individuals experience leptin resistance, elevated leptin levels, and a higher risk of hypertension. These findings suggest that squalene and its products could be beneficial in managing obesity, hypertension, and related metabolic disorders. Liu et al. (2009) studied the effects of high-dose squalene (1000 mg/kg for 4 weeks) on rats. They found that the squalene-fed rats had lower blood pressure, and reduced levels of leptin, blood glucose, cholesterol, and triglycerides. By day 75, these rats also had less body weight and body fat compared to the control group. Narayan Bhilwade et al. (2010) suggested that squalene may help leptin work better, which could reduce obesity and high blood pressure.

4. Health Benefits of Fish-Derived Squalene

4.1. Reduction in cardiovascular disease risk

Several studies have highlighted the potential role

of squalene in reducing the risk of cardiovascular diseases. Ibrahim et al. (2020) demonstrated that supplementation with fish-derived squalene led to significant improvements in lipid profiles and reduced oxidative stress markers, which are both linked to a lower risk of cardiovascular disease. Moreover, squalene has shown promise in reducing hypertension, a major risk factor for cardiovascular disease.

4.2. Reduction of atherosclerosis

Atherosclerosis, the buildup of plaque inside the arteries, is one of the leading causes of heart attacks and strokes. Squalene has been shown to reduce the formation of atherosclerotic plaques in animal models. The antioxidant and cholesterol-lowering effects of squalene, combined with its ability to modulate inflammatory processes, help to maintain arterial health and prevent plaque buildup (Indrawan, 2023).

4.3. Regulation of blood lipids

As mentioned, squalene has demonstrated an ability to regulate blood lipids, particularly by lowering total cholesterol, LDL cholesterol, and triglycerides. Elevated levels of LDL cholesterol and triglycerides are major contributors to the development of atherosclerosis and heart disease. By promoting a healthy lipid profile, squalene reduces the likelihood of plaque formation in blood vessels and lowers the risk of heart attack and stroke.

4.4. Support of heart function

Beyond its lipid-lowering effects, squalene has shown potential benefits for heart function. It helps in maintaining optimal heart function by reducing oxidative stress and supporting healthy blood flow. By enhancing the delivery of oxygen and nutrients to cardiac tissues, squalene may help protect the heart from ischemic damage.

5. Scientific Evidence Supporting Squalene's Cardioprotective Role

Squalene concentrations in human tissues also varies from tissue to tissue, where the highest levels were found in skin and adipose tissue, while only moderate amounts were found in liver and intestine which are the sites of active cholesterol synthesis (Liu et al., 1976). Squalene is located in the middle of the lipid bilayer, where it helps stabilize cell and membrane layers by forming complexes with fatty acids. This unique distribution may make the heart muscle more resistant to oxidative damage.

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The Farvin group from India researched the impact of squalene in rats with isoprenaline-induced myocardial infarction. They found that giving 2% squalene in the feed for 45 days helped prevent changes in key enzymes and maintained normal levels of amino acids and proteins in the heart tissue. Numerous studies have demonstrated the cardiovascular benefits of squalene derived from fish oils. In human trials, squalene supplementation has been shown to improve lipid metabolism and reduce oxidative stress markers, suggesting its role in preventing cardiovascular diseases (Kelly, 1999). Squalene is not only a bioactive compound which plays an important role in reducing inflammatory mediators but also helps in increasing energy production which can be effective and useful in reducing the consequences of type 2 diabetes mellitus (Martirosyan et al., 2022).

6. Conclusion

Fish-derived squalene represents a potent, natural compound with significant cardiovascular benefits. Its antioxidant properties, ability to regulate cholesterol and lipids, anti-inflammatory effects, and support of endothelial function all contribute to its role as a cardio-protector. As the research on squalene continues to expand, its potential as a therapeutic agent for cardiovascular health becomes increasingly evident. However, further human clinical trials are needed to solidify its benefits and establish optimal dosages for cardiovascular disease prevention and treatment.

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