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Review Article

Evaluating the Impact of CoQ10 on Dyslipidemia and Statin-induced Myopathy: A Systematic Review on Clinical Trials

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A B S T R A C T

Elevated cholesterol levels pose an increased risk for heart disease and stroke contribute to the burden of ischemic heart disease cases and affect around 39% of adults globally. This study focuses on exploring the potential benefits of Coenzyme Q10 (CoQ10) alone and in combination therapy in reducing high cholesterol levels. This study also addresses the effectiveness of CoQ10 in managing statin-associated myopathy. By conducting a systematic review, we compiled and analyzed relevant clinical data obtained from five articles on CoQ10 solo therapy and eleven articles on CoQ10 combination therapy and its effects on elevated cholesterol levels. Six articles were assessed on the effectiveness of CoQ10 to reduce Statin-Associated Myopathy symptoms. All articles were sourced through PubMed. Initial findings suggest a positive impact of using CoQ10 supplementation in solo and combination therapy to impact cholesterol levels. As both formulations show promise, evidence that CoQ10 in combination with substances such as red yeast rice, berberine, and monacolin K is superior. All twelve studies from the combination analysis had a positive impact on patient's lipid panels. Further research is needed to establish more definitive conclusions regarding its efficacy in managing statin-associated muscle pain as results were conflicting.

Keywords: Coenzyme Q10, Monacolin K, Berberine, Hyperlipidemia, Statin Associated Myopathy, Systematic Review.

Introduction

Dyslipidemia refers to an abnormal amount of lipids (fats) in the blood, including cholesterol and triglycerides [1]. High cholesterol is a common condition affecting a significant portion of the world's population. According to the World Health Organization (WHO), around 39% of adults (37% for males and 40% for females) had raised total cholesterol levels [2]. In the United States, an estimated 86 million adults age 20 or older have total cholesterol levels above 200 mg/dL, making it one of the leading countries with this health issue [3]. Elevated cholesterol levels can lead to various health complications, including an increased risk of developing cardiovascular diseases such as heart attacks and strokes [4]. An increased cholesterol level also contributes to a higher 10-year ASCVD score.

Statin medications are commonly prescribed by doctors to manage high cholesterol levels due to

their effectiveness in lowering LDL (bad) cholesterol. Statins can reduce the risk of cardiovascular events effectively [5]. However, statins are associated with potential side effects, including statin-associated myopathy. Statin-associated myopathy is a condition characterized by muscle pain, weakness, and inflammation [6]. Research indicates that statin-associated myopathy occurs in approximately 29% of patients taking statin therapy with varying degrees of severity [7].

Managing cholesterol levels through lifestyle modifications and medication is crucial in reducing these risks and improving overall health outcomes. Healthcare providers need to monitor patients for symptoms of myopathy and consider alternative treatment options if necessary to ensure the best outcomes for individuals with high cholesterol. Coenzyme Q10, often abbreviated as "CoQ10", is a dietary supplement that plays a crucial role in generating energy in the cells and acts as a powerful antioxidant in the body [8,9]. It is commonly used as a dietary supplement to support heart health [10]. CoQ10 can be found naturally in various foods such as fish, nuts, seeds, fruits, and vegetables [11]. Increasing your intake of these foods can help increase your levels of CoQ10 naturally. The review seeks to provide valuable insights into the potential benefits of CoQ10 in managing dyslipidemia and addressing the side effects associated with statin use.

Method

An SR was performed using the electronic database PubMed. The keywords "Coenzyme Q10, High Cholesterol" were used and the results were evaluated for appropriateness. The search produced 38 articles for high cholesterol studies. The statin-associated myopathy search produced 19 total articles. For inclusion in this article, the study had to have CoQ10 as a treatment in the trial (Fig. 1).

Results and Discussion

In this article, we have organized three tables to provide a comprehensive overview of research on CoQ10 supplementation in patients with high cholesterol. Table 1 focuses attention on the effects

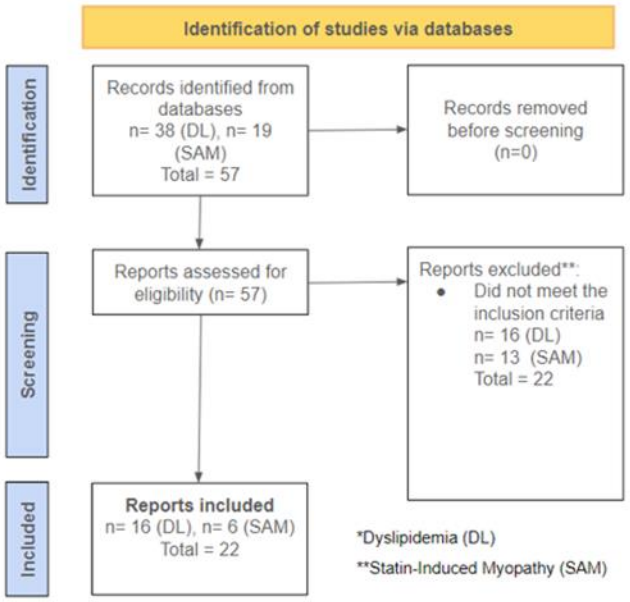

Figure 1: Flow Chart and Study Selection showing the number of articles identified after the initial keyword search and the number of articles included after the final screening.

of CoQ10 supplementation in high-cholesterol patients through clinical trials using only CoQ10. In Table 1, the findings suggest that in three out of the five studies, CoQ10 has a positive effect on cholesterol levels when in solo therapy.

Table 2 analyzes studies on the impact of combination products containing CoQ10 on cholesterol levels. In Table 2, the findings suggest positive evidence in all eleven studies. CoQ10, when used in combination with other supplements such as monacolin K, red yeast rice, berberine, folic acid, and many other compounds, has a positive benefit on dyslipidemia. Lastly, Table 3 presents clinical trials that explore the effects of CoQ10 supplementation in patients experiencing statin-associated myopathy symptoms. These tables aim to offer insight into the potential benefits of CoQ10 in managing high cholesterol and related symptoms.

The most common components used with CoQ10 were monacolin K, red yeast rice, and berberine. The combination of these products showed a very positive effect in reducing cholesterol levels. CoQ10 doses ranged from 2 mg - 50 mg in the different

Table 1: Effect of CoQ10 Supplementation in Patients with High Cholesterol

Study/Year	Daily Dose	Participants/ Duration	Outcomes
Derosa, Giuseppe et al. 2019 [31]	100 mg/day	50/1 Month	✅ CoQ10 in addition to half dosage statin in patients with previous intolerance to statins improves clinical symptoms such as asthenia, myalgia, or pain.
Taylor, Beth A et al. 2015 [32]	600 mg/day	120/8 Weeks	⛔ CoQ10 did not reduce muscle pain in patients with statin-induced myalgia.
Skarlovnik, Ajda et al. 2014 [33]	100 mg/day	50/30 Days	✅ CoQ10 effectively reduced statin-related mild-to-moderate muscular symptoms.
Fedacko, Jan et al. 2013 [34]	200 mg/day	60/1 Month	✅ CoQ10 decreased in the symptoms of SAM.
Caso, Giuseppe et al. 2007 [35]	100 mg/day	318/30 Days	✅ CoQ10 may decrease muscle pain associated with statin treatment.
Young, Joanna M et al. 2007 [36]	200 mg/day	44/12 Weeks	⛔ CoQ10 did not improve statin tolerance or myalgia.

Table 2: Combination Products Containing CoQ10 and Their Effect on Cholesterol Levels

Study/Year	Daily Dose	Participants/ Duration	Outcomes/Cholesterol Levels
Zou, Jinchao et al. 2022 [12]	120 mg	101, 24 Weeks	✅ CoQ10 significantly improves HDL-mediated CEC and the anti-inflammatory function of HDL in patients with dyslipidemia.
Sangouni, Abbas Ali et al. 2022 [13]	60 mg	88,12 Weeks	⛔ Coenzyme Q10 did not show any therapeutic benefit in subjects with metabolic syndrome.
Zhang, Peiwen et al. 2018 [14]	120 mg	101, 24 Weeks	✅ CoQ10 effectively reduced triglyceride and low-density lipoprotein cholesterol.
Gholnari, Tahereh et al. 2018 [15]	100 mg	50, 12 Weeks	⛔ CoQ10 did not have any benefit and patients had unchanged lipid profiles.
Shojaei, Mirhatef et al. 2011 [16]	100 mg	52, 3 Months	✅ CoQ10 did reduce serum levels of lipoprotein(a) in maintenance hemodialysis patients treated with statins.

combination products in the trials in this SR. Monacolin K is structurally identical to the medicine lovastatin. Traditional red yeast rice may contain trace amounts of monacolin K (lovastatin) [28]. Monacolin K levels can be difficult to determine in commercial red yeast rice products. The studies in this SR mostly utilized a 10 mg equivalent dose of monacolin K. Berberine is also a dietary supplement used for many medical conditions. Berberine is most well-known for helping manage diabetes [29]. When berberine is used in combination with other products, it has been shown to have efficacy in managing cholesterol levels [30]. The dose range for berberine in the studies analyzed in this SR was 500 mg. The combination of these products with the addition of more mentioned in the table in the methods section proved to be effective in reducing cholesterol levels. The combination products were shown to be superior to taking CoQ10 in solo therapy.

Table 3: Effect of CoQ10 supplementation in patients with SAMS

Study/Year	Combination	Participants /Duration	Outcomes
Angelopoulos, Nicholas et al. 2023 [17]	Monacolin K (3 mg/10mg) combined with Coenzyme Q10 (2 mg), Grape Seed, (50 mg) Olive Leaf Extracts (50 mg), and Vitamin B1, B2, B5 & B6	105, 8 weeks	✅ This combination product provided LDL-C-lowering properties.
Martinez-Martin, F et al. 2022 [18]	3.75mg of Monacolin K, 515mg of Berberine and 50mg of Coenzyme Q10 per tablet	3 months	✅ This combination is effective and safe for treating patients with hypercholesterolemia.
Mazza, Alberto et al. 2019 [19]	Red Yeast Rice, Berberine, Coenzyme Q10, Folic Acid, and Chrome	66, 3 months	✅ This combination is effective in improving lipid patterns.
Ruscica, Massimiliano et al. 2019 [20]	1 bn UFC Bifidobacterium longum BB536, RYR extract (10 mg Monacolin K), 16 mg Niacin, 20 mg Coenzyme Q10	33, 12 weeks	✅ This combination significantly improved in patient's atherogenic lipid profile.
Mazza, Alberto et al. 2018 [21]	10 mg of Monacolin K and 30 mg of Coenzyme Q10	104, 2 months	✅ This combination is safe, well tolerated, and effective in improving patient's lipid profiles.
Magno, S et al. 2018 [22]	Red Yeast Rice Extract 200 mg,(corresponding to Monacolin K 10 mg), Citrinine and Aflatoxin-Free; L-Arginine 3500 mg; Coenzyme Q10 50 mg; Ascorbate 100 mg. Red Yeast Rice Extract 200 mg(corresponding to Monacolin K 10 mg); Gamma Orizanol 90 mg; Coenzyme Q10 10 mg; Polycosanols 5 mg; Chrome Picolinate 0.2 mg.	20, 12 weeks	✅ Produces a significant reduction of triglycerides without significant effects on HDL.
D'Addato, Sergio et al. 2017 [23]	RYR (Monacolin K 10 mg), Berberine (500 mg), Coenzyme Q10 (2 mg), and Hydroxytyrosol (5 mg)	158, 4 weeks	✅ This combination showed good efficacy and safety profile and it can be considered an alternative to pharmacological treatment for patients with mild-to-moderate hypercholesterolemia.
Cicero, Arrigo Francesco Giuseppe et al. 2017 [24]	500 mg of Artichoke Extract, 200 mg of Red Yeast Rice (corresponding to 10 mg of Monacolin K), 75 mg of Banaba Extract, 50 mg of Coenzyme Q10, 9 mg of Vitamin B3, 1.4 mg of Vitamin B6, 0.83 mcg of Vitamin B12, 110 mcg of Folic Acid	30, 6 weeks	✅ This combination has shown clinical efficacy in the reduction of total cholesterol, non-HDL, LDL, and triglycerides
Cicero, Arrigo F G et al. 2016 [25]	10 mg Monacolins and 30 mg Coenzyme Q10	40, 4 weeks	✅ This combination is associated with an improvement in LDL-cholesterolemia in moderately hypercholesterolemic subjects.
Mazza, Alberto et al. 2015 [26]	NC-containing Red Yeast Rice, Policosanol, Berberine, Folic Acid, and Coenzyme Q10	66, 6 months	✅ This combination was found to be safe, well tolerated, and effective in improving lipid patterns.
Ruscica, Massimiliano et al. 2014 [27]	200 mg of RYR [equivalent to 3 mg of Monacolin K], 500 mg of Berberine, 10 mg of Policosanols, 0.2 mg of Folic Acid, 2.0 mg of Coenzyme Q10, and 0.5 mg of Astaxanthin	30, 8 weeks	✅ This combination showed lipid-lowering activity comparable to pravastatin treatment.

This study aims to investigate whether replenishing CoQ10 could help with SAMS or provide benefits to patients seeking relief from associated pain. The results from clinical trials of CoQ10 revealed mixed findings. Some studies indicated no impact of CoQ10 supplements on SAMS, while others reported a positive benefit in the symptom reduction of SAMS cases. These conflicting outcomes provide an uncertain conclusion on the efficacy of CoQ10 supplementation for SAMS. Research suggests that the CoQ10 pathway is not the most important for the development of SAMS [37]. Another study on 18 patients suggests that statin drug-related myopathy is associated with a mild decline in muscle CoQ10 concentration [38]. Another meta-analysis supports the use of exogenous CoQ10 in SAMS [39]. In Table 3, the findings suggest in four out of six studies that supplementation with CoQ10 does help with the symptoms of statin-associated myopathy.

Conclusion

In conclusion, CoQ10 has potential because of its antioxidative properties and involvement in cellular energy production. Although studies indicate that CoQ10 supplementation may enhance the overall cholesterol profile, it is important to note that it should complement rather than replace prescribed medications or medical advice. Individuals with elevated cholesterol levels should speak with their healthcare provider to evaluate the potential advantages and drawbacks of CoQ10 supplementation within their treatment plan. Regarding CoQ10 use in addressing statin-associated muscle pain, more extensive research is needed to establish definitive outcomes. Future clinical trials are necessary to determine the optimal dosages of CoQ10 supplementation. It is worth noting that CoQ10 supplements are not endorsed by the U.S. Food and Drug Administration for treating any medical condition. Seeking advice from a healthcare professional before initiating any new supplement routine is recommended.

Conflict of interest

The authors declare no conflict of interest.

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