GSC Advanced Research and Reviews

eISSN: 2582-4597 CODEN (USA): GARRC2

Cross Ref DOI: 10.30574/gscarr

Journal homepage: https://gsconlinepress.com/journals/gscarr/

(REVIEW ARTICLE)

Check for updates

Coenzyme Q10 in Preclinical Research: Comprehensive Review of Mitochondrial Mechanisms, Therapeutic Potential and Translational Challenges

Sai Harsha Vardhan Joga, Abhinaya Baka, Thanuja Bondapalli and Swathi Putta *

Department of Pharmacology, Raghu College of Pharmacy, Dakamarri, Visakhapatnam, 531162, Andhra Pradesh, India.

GSC Advanced Research and Reviews, 2025, 25(03), 188-199

Publication history: Received on 06 November 2025; revised on 10 December 2025; accepted on 13 December 2025

Article DOI: https://doi.org/10.30574/gscarr.2025.25.3.0385

Abstract

Coenzyme Q_{10} (CoQ10), or ubiquinone/ubiquinol, is an essential lipid-soluble quinone with central roles in mitochondrial electron transport and antioxidant defence. Over several decades, extensive preclinical research has established CoQ10 as a bioenergetic and cytoprotective molecule with relevance across diverse disease models, including cardiac ischemia–reperfusion injury, heart failure, neurodegenerative disorders such as Parkinson's disease, diabetes-associated organ damage, and primary mitochondrial disorders involving CoQ biosynthesis defects. Mechanistic investigations demonstrate that CoQ10 improves mitochondrial respiration, restores ATP synthesis, reduces reactive oxygen species, stabilizes membranes, influences mitophagy, and modulates redox-sensitive signalling pathways. Novel formulations developed to overcome poor oral bioavailability—such as ubiquinol, nano-CoQ10, liposomal preparations, and mitochondrial-targeted derivatives like MitoQ—show dramatically enhanced efficacy in experimental systems. Despite strong preclinical evidence, translation to clinical outcomes has been inconsistent, largely due to limitations in delivery, dosing, and model relevance.

Keywords: Coenzyme Q_{10}; Ubiquinol; Mitochondria; Novel formulations; Preclinical

1. Introduction

Coenzyme Q_{10} (CoQ_{10}) has been reported to reduce the anticoagulant effect of warfarin in some patients, producing a fall in prothrombin time / INR that, in case reports, has reverted after stopping CoQ_{10} (Landbo, 1998). The hypothesized mechanistic basis is twofold: (1) a structural similarity of ubiquinone/ubidecarenone to vitamin K (menaquinone) that could exert vitamin-K-like procoagulant activity or compete in related biochemical pathways, and (2) possible effects on hepatic warfarin metabolism (altering hydroxylation/clearance) described in preclinical microsomal studies although enzymatic mechanisms are not fully established in humans (Bentinger, Tekle, & Dallner, 2010; Landbo, 1998; research on warfarin hydroxylation suggests potential effects in microsomes). Because the mechanism is not definitively proven, the interaction is best characterized clinically as possible and idiosyncratic rather than uniform or predictable (Bentinger et al., 2010; Ge et al., 2014). Clinical evidence is mixed. Several case reports describe clinically meaningful INR decreases temporally associated with initiation of CoQ_{10} and normalization of INR after discontinuation (Landbo, 1998; Ge et al., 2014). By contrast, at least one small randomized, double-blind, placebo-controlled crossover trial (24 stable warfarin patients given 100 mg CoQ_{10} daily) did not find a statistically significant effect on PT/INR over the study period (Engelsen et al., 2003), and larger systematic reviews of herb/supplement-warfarin interactions emphasize limited and variable evidence for CoQ_{10} (Holbrook et al., 2005; Tan et al., 2021). Taken together, the literature supports that CoQ_{10} can reduce INR in some patients, but the effect is inconsistent and not reliably dose-dependent across studies (Landbo, 1998; Engelsen et al., 2003; Ge et al., 2014). When the interaction occurs, the magnitude can be clinically important (case reports document drops from therapeutic INR to subtherapeutic ranges), which could increase the risk of thrombosis if unrecognized (Landbo, 1998). The effect generally appears reversible

* Corresponding author: Swathi P

after discontinuation of CoQ_{10} (Landbo, 1998; Ge et al., 2014). No high-quality large RCTs are demonstrating a predictable dose–response or defining the approximate risk across populations; therefore, the strength of evidence is low–moderate and largely based on case reports, small trials, and pharmacologic rationale (Holbrook et al., 2005; Bentinger et al., 2010).

2. Rationale for preclinical research on CoQ10:

Preclinical models have been essential in understanding how CoQ10 functions in disease and recovery. They illustrate that CoQ10, Coenzyme Q10 plays a vital role in maintaining mitochondrial integrity and cellular health. It corrects mitochondrial dysfunction in conditions where the electron transport chain is impaired and restores ATP levels in energy-deprived tissues (Hernández-Camacho, García-Corzo, Moreno-Fernández-Ayala, & Navas, 2021; Mantle, 2024). Additionally, CoQ10 reduces mitochondrial reactive oxygen species generated during ischemic, inflammatory, or toxic states, helping to stabilize mitochondrial membranes and prevent the opening of the permeability transition pore (Suárez-Rivero et al., 2021; Papucci et al., 2003). Through these actions, it enhances key cell-survival signaling pathways, mitigates inflammation, and supports tissue repair (Xie et al., 2020; Chen et al., 2024). Emerging evidence also shows that CoQ10 modulates mitophagy and mitochondrial turnover, thereby promoting the renewal of healthy mitochondria (Rodríguez-Hernández et al., 2009; Hidalgo-Gutiérrez et al., 2021). Together, these diverse biological effects observed in preclinical studies provide the rationale for its investigation across a wide range of disease conditions (Mantle, 2024; Hernández-Camacho et al., 2021). Although preclinical evidence is extensive, the information is often fragmented across subdisciplines—cardiology, neurology, nephrology, endocrinology, and mitochondrial biology. A unified synthesis is valuable because CoQ10's mechanism is fundamentally mitochondrial, and many diseases share mitochondrial dysfunction as a core pathogenic feature (Mantle, 2024; Neergheen, 2017; Wen et al., 2025; Barcelos & Navas, 2019).

Furthermore, the substantial discrepancies between the robust success observed in preclinical studies and the mixed outcomes reported in clinical trials highlight the need for a critical evaluation of several key factors. These include the selection of appropriate experimental models, the dosing strategies employed, and the specific formulations of CoQ10 used across studies. Equally important are considerations related to tissue delivery efficiency, the relevance and sensitivity of outcome metrics, and the broader translational bottlenecks that may hinder successful movement from bench to bedside. Together, these elements must be scrutinized to better understand the inconsistencies in therapeutic outcomes and to optimize the clinical development of CoQ10 (Pastor-Maldonado et al., 2020; Mantle, 2020; Fratter et al., 2025; Zaki & Burt, 2016).

Coenzyme Q10 (ubiquinone/ubiquinol) functions as a mobile electron carrier within the inner mitochondrial membrane. It transfers electrons from Complex I (NADH:ubiquinone oxidoreductase) and Complex II (succinate dehydrogenase) to Complex III (cytochrome bc_1) as part of the mitochondrial respiratory chain (Hidalgo-Gutiérrez et al., 2021; Suárez-Rivero et al., 2021; Nolfi-Donegan et al., 2020). This process, commonly referred to as the Q-cycle, involves several coordinated molecular steps in mitochondrial electron transport (Lenaz & Genova, 2009; Hernández-Camacho, 2021).

Coenzyme Q10 (ubiquinone/ubiquinol) functions as a mobile electron carrier within the inner mitochondrial membrane. It is initially reduced to ubiquinol ($CoQ10H_2$) via electrons derived from NADH at Complex I and $FADH_2$ at Complex II. The resulting ubiquinol then diffuses laterally across the inner mitochondrial membrane to reach Complex III, where it is oxidized, releasing two electrons into the cytochrome *c* pathway and pumping protons into the intermembrane space. The return of ubiquinone completes the cycle, enabling continuous electron transfer. Through this mechanism, CoQ10 directly regulates the proton-motive force, maintains mitochondrial membrane potential ($\Delta\Psi m$), supports ATP synthesis, and ensures efficient electron flux throughout the electron transport chain. Dysfunction in any of these steps leads to electron leakage and reactive oxygen species (ROS) production, particularly at Complexes I and III. CoQ10 deficiency amplifies this leakage, while supplementation normalizes electron transfer in deficient mitochondria (Nolfi-Donegan et al., 2020; Enriquez et al., 2014; Cornelius et al., 2013).

2.1. Key antioxidant functions:

$CoQ10H_2$ plays a critical role in lipid peroxidation defence by preventing oxidative damage to key cellular and mitochondrial structures. It protects mitochondrial membrane cardiolipin, maintains the integrity of phospholipid bilayers, safeguards circulating low-density lipoprotein (LDL) particles from oxidation, and preserves the function of membrane-bound proteins. Through these actions, $CoQ10H_2$ helps maintain cellular and mitochondrial stability under conditions of oxidative stress. Its antioxidant role is uniquely efficient due to its high concentration in membrane

interiors, where polyunsaturated fats are most vulnerable (Hidalgo-Gutiérrez et al., 2021; Lokhmatikov, Bubnov & Nadezhdin, 2014; Zozina & Pernow, 2018; Navas et al., 2005; Samimi et al., 2024).

CoQ10 also plays a pivotal role in maintaining the antioxidant network within cells by regenerating other key antioxidants. It facilitates the recycling of vitamin E (α-tocopherol), vitamin C (ascorbate), and reduced glutathione (GSH), thereby enhancing their capacity to neutralize reactive oxygen species and sustain cellular redox balance. By cooperating with these antioxidant systems, CoQ10 becomes central to redox homeostasis (Signorini et al., 2017; Mantle et al., 2025).

Several studies have demonstrated that CoQ10 influences key transcriptional pathways involved in mitochondrial function. Notably, it enhances the expression of PGC-1α, a master regulator of mitochondrial biogenesis, through activation of AMPK and SIRT1-mediated deacetylation (Xu et al., 2017; Stone et al., 2019; Mantle et al., 2025). By modulating these pathways, CoQ10 promotes the formation of new mitochondria and supports cellular energy metabolism (Xu et al., 2017; Mantle et al., 2025).

CoQ10 activates the nuclear factor Nrf2, a key regulator of cellular antioxidant defenses, which in turn induces the expression of antioxidant-response elements (ARE) including HO-1, superoxide dismutase (SOD), and glutamate–cysteine ligase catalytic subunit (GCLC). Through this pathway, CoQ10 enhances the cell's capacity to neutralize reactive oxygen species and maintain redox homeostasis (Samimi et al., 2024; Mantle et al., 2025; Pala et al., 2016). This expands its role beyond bioenergetics into genetic regulation of antioxidant defenses.

2.1.1. Stabilization of Mitochondrial Membranes

CoQ10 interacts closely with cardiolipin, a phospholipid unique to the mitochondrial membrane, to support mitochondrial structure and function. This interaction helps maintain membrane fluidity, stabilizes protein complexes within the electron transport chain, and protects cardiolipin from oxidative damage (Seychell et al., 2025; Paradies, Paradies & Ruggiero, 2014; Suárez-Rivero et al., 2021). Additionally, CoQ10 prevents the dissociation of cytochrome c and limits mitochondrial apoptotic signaling, thereby contributing to cellular survival and mitochondrial integrity (Zhong et al., 2017; Papucci et al., 2003). This membrane-protective effect is essential in tissues with high oxygen consumption (heart, kidney, liver, neurons) (Paradies, 2019; Camara et al., 2011).

2.1.2. CoQ10 and Mitochondrial Apoptosis Regulation

Mitochondria play a central role in regulating apoptosis through the release of cytochrome c and subsequent activation of caspases. CoQ10 mitigates pro-apoptotic signaling by maintaining mitochondrial membrane potential (ΔΨm), preventing the opening of the mitochondrial permeability transition pore (mPTP), reducing the Bax/Bcl-2 ratio, and inhibiting the activation of caspase-3 and caspase-9. Through these mechanisms, CoQ10 promotes cell survival and protects against mitochondrial-mediated apoptosis (Papucci et al., 2003; Lee et al., 2014; Al-Megrin et al., 2020; Marcheggiani et al., 2019). These anti-apoptotic mechanisms underlie the protective effects of CoQ10 observed in various disease models, including ischemia-reperfusion injury, Parkinson's disease, diabetic nephropathy, sepsis, and muscle wasting. By preventing mitochondrial-mediated cell death, CoQ10 helps preserve tissue integrity and function across these diverse pathological conditions (Mantle, Cufflin, Purcell & Hargreaves, 2025; Bagheri et al., 2023; Zhao et al., 2022; Boroujeni et al., 2017; Fakharaldeen et al., 2023).

2.1.3. Preclinical Studies of Coenzyme Q10 (In-Vitro and Animal Models)

In *in-vitro* studies on neuronal cells, human neuroblastoma (SH-SY5Y) and rat pheochromocytoma (PC12) cells supplemented with CoQ10 exhibited reduced reactive oxygen species (ROS) following rotenone exposure, restored Complex I activity, decreased α-synuclein aggregation, and improved ATP production. These findings highlight CoQ10's potential role in providing mitochondrial neuroprotection and its therapeutic relevance for Parkinson's disease (Millichap et al., 2024; Seidl & Potashkin, 2011; Sherer et al., 2003). In endothelial and cardiomyocyte models, cardiac-derived H9c2 cells exposed to oxidative stress demonstrated decreased lipid peroxidation, maintenance of mitochondrial membrane potential, and reduced apoptosis when treated with CoQ10 (Rizzardi et al., 2021; Yuan et al., 2023). Similarly, endothelial cells exhibited CoQ10-mediated protection against nitric oxide depletion, indicating potential benefits in conditions such as atherosclerosis and endothelial dysfunction (Tsai et al., 2012; Tsuneki et al., 2013; Suárez-Rivero et al., 2019).

2.1.4. Neurodegenerative Disease Models

In Parkinson's disease preclinical models, including rotenone- and MPTP-treated mice, CoQ10 supplementation has been shown to reduce dopaminergic neuronal loss, increase mitochondrial respiratory capacity, lower α-synuclein

accumulation, and decrease microglial activation (Beal et al., 1998; Moon et al., 2005; Sharma et al., 2006; Yang et al., 2009; Bagheri et al., 2023). Furthermore, nanoparticle and liposomal formulations of CoQ10 demonstrate enhanced blood–brain barrier penetration, improving its neuroprotective efficacy (Sikorska et al., 2014; Umer et al., 2025; Halder et al., 2025).

In Huntington's disease models — specifically in the R6/2 transgenic mice — Coenzyme Q10 (CoQ10) supplementation has been shown to delay motor function decline, reduce brain atrophy, and enhance mitochondrial enzyme activity (e.g., higher ATP, reduced oxidative damage). These promising preclinical results spurred clinical interest; however, subsequent human trials have produced mixed outcomes, with some showing no statistically significant slowing of functional decline in patients with Huntington's disease

2.1.5. Metabolic Disorders and Diabetes Models

CoQ10 supplementation in models of diabetic nephropathy, specifically STZ-induced diabetic rats, has been shown to reduce proteinuria, improve glomerular filtration, normalize mitochondrial morphology, and decrease NF-κB activation, indicating its potential to protect renal function under diabetic conditions (Mahajan et al., 2020; Zhang et al., 2019; Chen et al., 2018). In models of insulin resistance and obesity, particularly high-fat diet–fed mice, CoQ10 supplementation has been shown to improve insulin sensitivity, reduce hepatic steatosis, increase the expression of AMPK and PGC-1α, and decrease adipocyte inflammation (Chen et al., 2019; Sohet et al., 2009; Alam & Rahman, 2014; Dludla et al., 2020; Mantle et al., 2025). These findings underscore CoQ10's role in regulating mitochondrial metabolism and supporting metabolic health (Alam & Rahman, 2014; Dludla et al., 2020; Mantle et al., 2025).

2.1.6. CoQ10 in Mitochondrial Genetic Disorders

In models of primary CoQ_{10} deficiency including mutations in COQ2, COQ4 and PDSS1 (among other biosynthetic genes) genetic defects cause severe mitochondrial dysfunction, neuromuscular degeneration and renal/kidney failure (González-García et al., 2021; Mantle & Hargreaves, 2023; Staiano et al., 2023). Supplementation with CoQ_{10} — either ubiquinone or ubiquinol — partially restores mitochondrial electron transport and ATP synthesis, reduces lactic acidosis, and can ameliorate organ damage and extend survival in some of these models (González-García et al., 2021; Mantle & Hargreaves, 2023). However, due to limited uptake and poor tissue distribution of exogenous CoQ_{10} — especially in certain affected tissues — the therapeutic efficacy remains suboptimal, underscoring the need for improved formulations or delivery strategies (González-García et al., 2021; Staiano et al., 2023).

3. Liver and Kidney Protection Models

In hepatic injury models, CoQ_{10} has been shown to reduce mitochondrial oxidative damage caused by acetaminophen-induced toxicity, alcohol-induced hepatotoxicity, and CCl_4-induced liver injury. The protective mechanisms involve suppression of cytochrome P450 activation, enhancement of antioxidant enzyme activity, including superoxide dismutase (SOD) and catalase, and reduction of mitochondrial swelling, collectively contributing to improved liver mitochondrial function (Fouad & Jresat, 2012; Chen et al., 2021; Lamia et al., 2021; Hussein et al., 2021). In animal models of ischemic and nephrotoxic acute kidney injury, Coenzyme Q10 (CoQ_{10}) administration has been shown to reduce tubular necrosis, stabilize mitochondrial membranes, and lower serum creatinine and blood urea nitrogen (BUN), indicating a protective effect on renal function. For example, in a mouse model of acute renal injury induced by a single intraperitoneal injection of Cisplatin (5 mg/kg), CoQ_{10} treatment (10 mg/kg/day for 6 days, starting one day before cisplatin) significantly reduced elevated BUN and serum creatinine and markedly ameliorated histopathological renal damage including tubular necrosis, rescued antioxidant defenses (reduced glutathione and superoxide dismutase activity), suppressed lipid peroxidation, and lowered inflammatory and apoptotic markers such as inducible nitric oxide synthase, nuclear factor-κB, caspase-3, and p53.

Similarly, a recent review summarizing experimental acute kidney injury (AKI) models, including ischemia–reperfusion, drug-induced toxicity, and other insults concluded that CoQ_{10} exerts renoprotective effects by preserving mitochondrial integrity and function, mitigating oxidative stress and inflammation, and thereby helping maintain renal function under AKI conditions.

In rodent models of muscle fatigue and exercise physiology, supplementation with Coenzyme Q10 (CoQ10) has been shown to increase endurance time, reduce lactate accumulation, prevent mitochondrial dysfunction, and improve recovery following exhaustive exercise with benefits attributed to enhanced oxidative phosphorylation and reduction of reactive oxygen species (ROS) in muscle tissue. For example, in male ICR mice given CoQ10, exhaustive swimming time until exhaustion was significantly prolonged compared with controls, and post-exercise levels of lactate, ammonia and creatine kinase (CK) were dose-dependently reduced, while muscle and liver glycogen stores increased, indicating

enhanced energy availability and reduced fatigue (Chen et al., 2019). Furthermore, in mice assessed for the anti-fatigue effects of CoQ10, supplementation significantly improved endurance capacity compared with controls (Fu, Ji, & Dam, 2010). In another study, CoQ10 reversed reductions in exercise endurance and mitochondrial respiratory-chain capacity in mice treated with statins supporting a role of CoQ10 in preserving mitochondrial function and enhancing exercise performance under metabolic stress (Muraki et al., 2012).

3.1. Immune System and Inflammation Models

CoQ10 modulates immune function by inhibiting NF-κB signaling, reducing pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α, and stabilizing mitochondrial reactive oxygen species generation in immune cells. In mouse models of sepsis, early administration of CoQ10 has been shown to improve survival, highlighting its potential role in controlling inflammation and supporting immune resilience. Bessler, H., Cohn, J., Gonen, B., Grisaru, D., Lev, Z., Schulman, S., & Garty, M. (2010). In preclinical cancer biology models, CoQ10 has demonstrated potential anti-tumor effects, including inhibition of melanoma and breast cancer cell proliferation, enhancement of mitochondrial respiration in immune cells, and reduction of tumor growth rates in some xenograft mouse models. However, these findings remain preliminary and have not yet been validated in clinical studies. Li, Q., et al. (2020)

3.2. Clinical Studies of Coenzyme Q10

In cardiovascular disease, Coenzyme Q10 (CoQ10) has some of the strongest clinical evidence supporting its use particularly in heart failure. The landmark Q-SYMBIO trial (2014), a randomized, double-blind, placebo-controlled global multicentre study of 420 patients with chronic heart failure (NYHA Class III–IV) who received 100 mg of CoQ10 three times daily (total 300 mg/day) for two years, demonstrated a 43% relative reduction in major adverse cardiovascular events (MACE), a 44% reduction in cardiovascular mortality, significant improvement in NYHA functional class, and a reduction in hospitalisation rates (Mortensen et al., 2014). In earlier clinical trials of congestive heart failure (CHF) during the 1980s–2000s, supplemental Coenzyme Q10 (CoQ10) was associated with improvements in cardiac function — including increases in ejection fraction (EF), stroke volume (SV), cardiac output (CO), and cardiac index (CI) — along with reductions in left ventricular end-diastolic volume or diameter (LVEDV/LVEDD), and enhanced exercise tolerance and VO_2max (Soja et al., 1997; Rosenfeldt et al., 2003; Fotino et al., 2013). For example, Soja and colleagues found that CoQ10 supplementation in CHF patients resulted in improvements in SV, EF, CO, CI, and EDVI compared with placebo. A meta-analysis of randomized controlled trials similarly reported a net improvement of ∼3.7 % in EF in CoQ10-treated patients. Statins inhibit HMG-CoA reductase, which reduces synthesis of both cholesterol and endogenous CoQ10, contributing to mitochondrial dysfunction in skeletal muscle (Banach et al., 2018). Clinical studies in patients with statin-induced myopathy have shown that CoQ10 supplementation can reduce muscle pain, improve muscle strength, and lower creatine kinase (CK) levels, supporting its therapeutic role in muscle symptom relief (Caso et al., 2007; Qu et al., 2018). As a result, CoQ10 has become a commonly used adjunct therapy for managing statin intolerance, particularly in individuals who experience persistent myalgias while taking lipid-lowering therapy (Banach et al., 2018; Qu et al., 2018). Multiple randomized clinical trials investigating hypertension have shown that CoQ10 supplementation produces an average reduction of approximately 8–12 mmHg in systolic blood pressure, enhances endothelial nitric oxide production, and reduces vascular oxidative stress, demonstrating its vasoprotective effects (Hodgson et al., 2002; Rosenfeldt et al., 2007). A comprehensive meta-analysis of randomized controlled trials further confirmed that CoQ10 significantly lowers systolic blood pressure and improves endothelial function through enhanced NO bioavailability and reduced oxidative stress markers (Flores-Terry et al., 2021; Ho et al., 2020). Although the antihypertensive effect of CoQ10 is modest compared to standard drug therapies, the consistent findings across controlled studies support its use as an adjunctive therapy in managing hypertension (Ho et al., 2020; Flores-Terry et al., 2021).

In studies of atherosclerosis and endothelial dysfunction, CoQ10 has been shown to improve flow-mediated dilation (FMD), enhance the resistance of Low-density lipoprotein (LDL) to oxidation, and increase arterial compliance effects that collectively support its role in promoting long-term cardiovascular protection. For example, in a randomized trial among statin-treated type 2 diabetic patients with endothelial dysfunction, supplementation with 200 mg/day CoQ10 for 12 weeks significantly increased brachial artery FMD by ∼1.0% compared with placebo (Hamilton et al., 2009).

Similarly, a recent meta-analysis of randomized controlled trials found that CoQ10 supplementation significantly improved peripheral endothelial function assessed by FMD (standardized mean difference 1.70; 95% CI 1.00–2.40; $p < 0.0001$) but did not significantly affect nitrate-mediated dilation, suggesting a direct beneficial effect on endothelium-dependent vasodilation (Gao et al., 2012). In addition to effects on endothelial function, CoQ10 has been shown to decrease LDL oxidizability: a classic study in hypercholesterolemic subjects demonstrated that CoQ10 supplementation significantly increased the lag time before ex vivo oxidation of LDL and reduced accumulation of lipid peroxides, indicating enhanced antioxidant protection of LDL (Raitakari et al., 2000). Furthermore, in a double-blind randomized

trial of patients with ischaemic left-ventricular systolic dysfunction, supplementation with 300 mg/day CoQ10 for 8 weeks improved mitochondrial function (as indicated by reduced plasma lactate/pyruvate ratio) and increased FMD by 1.51% compared with placebo (Dai et al., 2011). Another more recent study showed that after 8 weeks of CoQ10 supplementation, endothelial function improved in a dose-dependent manner (Daei et al., 2024). These findings improved FMD, enhanced LDL resistance to oxidation, and improved arterial elasticity together support the notion that CoQ10 exerts beneficial vascular effects that may contribute to long-term cardiovascular protection.

3.3. Neurological Clinical Studies

In Parkinson's disease, early trials such as the one by Clifford W. Shults (2002) indicated that high-dose Coenzyme Q10 (CoQ10, 1200 mg/day) could slow disease progression in early, untreated patients, with those receiving the highest dose showing the least functional decline over 16 months (Shults et al., 2002). However, the subsequent 2014 Phase III QE3 trial found no significant clinical benefit at doses of 1200–2400 mg/day, leading to early termination for futility. Safety and tolerability were confirmed, but neither CoQ10 dose group showed a slower progression of symptoms compared with placebo (Beal et al., 2014). The lack of efficacy has been attributed by some authors to factors such as limited blood–brain barrier penetration, poor intracellular uptake, and the fact that intervention likely occurred at relatively late disease stages, when neurodegeneration had already advanced (Hung & Lee, 2020). Nevertheless, renewed interest has emerged in newer formulations including nanoparticles, liposomes, and micelles which aim to improve brain delivery and cellular uptake of CoQ10, thereby enhancing its therapeutic potential in Parkinson's disease (Park et al., 2020; Jiménez-Jiménez et al., 2022).

In Alzheimer's disease, clinical studies of CoQ10 have produced mixed results. Some small trials have reported improvements in oxidative stress biomarkers and modest cognitive benefits; for example, Galasko et al., 2012 found that antioxidant supplementation, including CoQ10, altered cerebrospinal fluid oxidative stress markers, although no significant changes in cognitive performance were observed. Larger systematic reviews similarly conclude that, while CoQ10 demonstrates neuroprotective effects in preclinical studies, no large-scale clinical evidence has confirmed its efficacy for cognitive improvement in Alzheimer's disease (Asadi et al., 2023). Notably, combination therapies appear more promising: in an Alzheimer-like rat model, co-administration of CoQ10 with omega-3 fatty acids led to enhanced reductions in oxidative stress, inflammation, and amyloid-β accumulation, supporting a potential synergistic effect for cognitive protection (Abd El-Fattah et al., 2020). These findings suggest that while standalone CoQ10 therapy remains inconclusive, integrating CoQ10 with other neuroprotective nutrients may provide greater therapeutic benefit in Alzheimer's disease management.

In Huntington's disease, a 2001 pilot study by the Huntington Study Group suggested that CoQ10 supplementation at 600 mg/day may slow functional decline, showing a trend toward delayed disease progression compared with placebo over 30 months (Huntington Study Group, 2001). However, a subsequent large-scale, high-dose Phase III clinical trial using 2,400 mg/day of CoQ10 (the 2CARE study) demonstrated no significant improvement in clinical outcomes, including functional capacity or mortality risk, ultimately leading to early study termination for futility (Huntington Study Group 2CARE Investigators, 2017). These findings highlight the challenge of translating neuroprotective effects observed in preclinical studies into meaningful clinical benefits for human patients with Huntington's disease. In migraine prevention, multiple controlled clinical trials have demonstrated that CoQ10 supplementation reduces headache frequency and duration while improving mitochondrial energy metabolism. A randomized, double-blind, placebo-controlled trial showed that 300 mg/day of CoQ10 significantly reduced the number of migraine attacks and headache days compared with placebo, with nearly half of the treated patients achieving at least a 50% reduction in attack frequency (Sandor et al., 2005). A meta-analysis of randomized controlled studies further confirmed that CoQ10 supplementation decreases monthly migraine frequency and shortens attack duration, supporting its role as an effective non-pharmacologic preventive therapy (Chen et al., 2021). Based on these results, CoQ10 at doses of 100–300 mg/day is now clinically recommended to help manage and prevent migraine episodes (Pringsheim et al., 2012).

3.4. Metabolic Disorders Clinical Studies

In type 2 diabetes, clinical studies indicate that CoQ10 supplementation can improve glycemic control by reducing HbA1c by approximately 0.3–0.6%, lowering fasting blood glucose levels, enhancing β-cell function, and decreasing oxidative stress markers. A meta-analysis of randomized controlled trials showed that CoQ10 significantly reduced both HbA1c and fasting glucose compared with placebo, suggesting improved insulin sensitivity (Suksomboon et al., 2019). Another dose–response meta-analysis reported additional benefits, including reductions in fasting insulin and HOMA-IR, indicating improved β-cell performance and glucose metabolism (Asadi et al., 2022). These effects appear to be most pronounced in patients with elevated oxidative stress, supporting CoQ10's mechanistic role in reducing oxidative damage and supporting pancreatic function in type 2 diabetes (Asadi et al., 2022; Suksomboon et al., 2019). In non-alcoholic fatty liver disease (NAFLD), randomized controlled trials have reported that CoQ10 supplementation can

reduce serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels, decrease hepatic steatosis, and lower inflammatory cytokine levels — effects attributed to enhanced mitochondrial oxidation and reduced lipid accumulation, supporting CoQ10's role in improving liver function and metabolic health. For example, a double-blind trial in NAFLD patients receiving 100 mg/day CoQ10 demonstrated significant improvements in systemic inflammation markers and liver biochemistry compared with placebo (Farsi et al., 2016). A 2024 randomized, double-blind, placebo-controlled trial found that six-month high-dose CoQ10 significantly reduced liver steatosis (as assessed by controlled-attenuation parameter on elastography), along with improvements in vascular and myocardial function (Vrentzos et al., 2024). Moreover, a recent meta-analysis of randomized controlled trials showed that CoQ10 supplementation significantly improved circulating ALT, AST, and GGT levels — suggesting a beneficial effect on hepatic enzyme abnormalities in NAFLD (Damaneh et al., 2023). Mechanistic reviews further propose that CoQ10's antioxidant and mitochondrial-supporting properties act to reverse oxidative stress and lipid peroxidation, thereby reducing hepatic fat accumulation and improving metabolic parameters (Casagrande et al., 2018).

In kidney disease clinical trials, CoQ10 supplementation has been shown to reduce serum creatinine levels, decrease oxidative stress, and lower proteinuria (Alehagen et al., 2020; Drovandi et al., 2022; Abe et al., 2024). In cases of primary CoQ10 deficiency nephropathy, particularly involving COQ2 and PDSS mutations, early CoQ10 supplementation dramatically improves outcomes, highlighting its critical role in preserving renal function (Peng et al., 2008; Tan et al., 2021; Mantle & Hargreaves, 2023). In clinical studies of mitochondrial disease, Coenzyme Q10 (CoQ10) supplementation has sometimes been reported to improve exercise capacity, reduce post-exercise lactate levels, and enhance mitochondrial enzyme activity, but the degree of benefit appears to vary depending on the specific genetic subtype of the disorder underscoring that individual genetic context strongly influences therapeutic outcomes. For example, in a randomized trial of patients with mitochondrial respiratory chain disorders, 60 days of moderate- to high-dose CoQ10 modestly increased VO_2/kg lean mass during cycling exercise and attenuated the post-exercise rise in lactate, although it did not significantly improve muscle strength or resting lactate levels (Glover et al., 2010). In a case report of a patient with isolated primary CoQ10-deficient myopathy, CoQ10 therapy resulted in clinical improvement, normalization of serum creatine kinase and lactate values, and reduced exercise intolerance (Lalani et al., 2005). Nevertheless, as pointed out in a comprehensive review, CoQ10's efficacy across mitochondrial (MRC) disorders remains inconsistent: while some patients benefit, others show little or no functional improvement, likely because of heterogeneity in genetic defects, disease severity, and differences in CoQ10 bioavailability, dosage, and treatment duration (Hargreaves & Mantle, 2014).

In human studies, CoQ10 supplementation has been shown to reduce inflammatory biomarkers — including C-reactive protein (CRP), IL-6, and TNF-α while improving mitochondrial function in immune cells. A meta-analysis of randomized controlled trials demonstrated significant reductions in CRP, IL-6, and TNF-α following CoQ10 supplementation, indicating a systemic anti-inflammatory effect (Zhang et al., 2017). More recent pooled clinical evidence further confirmed that CoQ10 improves inflammatory status and oxidative balance in metabolic and immune-related disorders (Fiorenza et al., 2023). Additionally, clinical studies in chronic fatigue syndrome and post-viral fatigue have shown that CoQ10 improves mitochondrial bioenergetics and reduces fatigue severity, supporting its role in restoring immune-energy function (Castro-Marrero et al., 2021). Due to these combined anti-inflammatory and mitochondrial-supportive benefits, CoQ10 is increasingly used as an adjunct therapy in conditions such as sepsis, chronic fatigue syndrome, and post-COVID-19 syndrome (Castro-Marrero et al., 2021; Fiorenza et al., 2023).

CoQ10 supplementation has been shown to enhance both male and female fertility by improving mitochondrial function in reproductive cells. In men, multiple clinical studies demonstrate that CoQ10 significantly increases sperm motility and concentration while boosting mitochondrial enzyme activity and antioxidant protection within spermatozoa (Lafuente et al., 2013). A systematic review further confirmed consistent improvements in semen parameters across treated individuals, supporting CoQ10 as an effective therapy for male infertility (Hughes et al., 2021). In women, randomized controlled trials have shown that CoQ10 supplementation improves ovarian response, increases the number of retrieved mature oocytes, and enhances embryo quality in individuals with diminished ovarian reserve, with measurable improvements in biomarkers such as AMH and antral follicle count (AFC) (Xu et al., 2018). A recent meta-analysis also found that CoQ10 supplementation improves clinical pregnancy rates in assisted reproductive technology (ART) cycles, reinforcing its clinical role in fertility optimization (Flourou et al., 2020). As a result of these combined findings, CoQ10 is widely used in fertility clinics to support reproductive health in both men and women.

3.5. Pharmacokinetics and Bioavailability:

CoQ10 is a lipophilic compound with a relatively large molecular weight, properties that limit its water solubility and slow its absorption from the gut (Sood et al., 2024; Mantle & Dybring, 2020). Its uptake occurs via incorporation into micelles in the intestine, followed by transport in chylomicrons through the lymphatic system into the circulation (Miles

et al., 2007; Mantle & Dybring, 2020). Several studies have shown that the reduced form, ubiquinol, exhibits higher bioavailability compared to oxidized ubiquinone under certain conditions — in some trials, ubiquinol produced higher plasma CoQ10 levels (Evans et al., 2009; Zhang et al., 2018), making it more efficiently absorbed in many clinical contexts. At the same time, the overall bioavailability of CoQ10 is highly dependent on formulation — crystal dispersion and carrier lipids/excipients can affect absorption more than whether the supplement is ubiquinone or ubiquinol (López-Lluch et al., 2019; Mantle & Dybring, 2020).

4. Safety, Toxicity, and Drug Interactions

Clinical trials administering CoQ10 at doses up to 3,000 mg/day have reported no major adverse effects, with only mild gastrointestinal symptoms observed in some cases. Its status as an endogenous compound contributes to an extremely favorable safety profile, even with long-term use.

Drug Interactions Statins, which inhibit HMG-CoA reductase to lower cholesterol synthesis, also inadvertently reduce endogenous CoQ10 production, as both cholesterol and CoQ10 share a common biosynthetic pathway. This reduction can contribute to statin-associated side effects, particularly muscle-related symptoms such as myalgia and fatigue. Supplementation with CoQ10 has been shown to restore normal CoQ10 levels, support mitochondrial function, and alleviate these adverse effects, making it a valuable adjunct therapy for patients experiencing statin intolerance. CoQ10 supplementation may slightly reduce the international normalized ratio (INR) in patients taking warfarin, likely due to its structural similarity to vitamin K, which plays a key role in the coagulation cascade. Although this effect is generally modest, it can influence anticoagulation control, making careful monitoring of INR essential when initiating or adjusting CoQ10 therapy in patients on warfarin. Clinicians should be aware of this potential interaction to ensure therapeutic anticoagulation is maintained and to minimize the risk of bleeding or thrombotic complications. Langsjoen PH et al. Statin-associated myopathy and CoQ10. Biofactors. 2003

4.1. Recommended Clinical Dosing

Table 1 Recommended dose of CoQ10 for various health conditions

Condition	Dose Range
Cardiovascular disease	100 – 300 mg/day
Heart failure	300 mg/day (Q-SYMBIO protocol)
Satin myopathy	100 – 200 mg/day
Parkinson’s	300 – 1200 mg/day
Migraine	100 – 300 mg/day
Diabetes	100 – 200 mg/day
Fertility	200 – 400 mg/day
Mitochondrial disorders	300 – 1200 mg/day
Anti–aging	100 – 200 mg/day

Despite extensive research on CoQ10, several limitations and challenges remain. Its poor solubility and limited absorption pose significant obstacles for oral formulations, often resulting in variable bioavailability. Additionally, CoQ10 exhibits limited central nervous system penetration, which likely contributes to the mixed results observed in neurological disease trials. Many clinical studies also administer CoQ10 after disease onset, potentially reducing its therapeutic impact. Furthermore, heterogeneity among commercially available formulations means that not all products provide equivalent bioavailability, complicating both clinical interpretation and consistent therapeutic outcomes. Future directions for CoQ10 research and therapy focus on improving delivery, efficacy, and targeted action. Advanced nanocarriers and intranasal formulations are being explored to enhance absorption and central nervous system penetration, while blood–brain barrier-permeable derivatives aim to improve neurological outcomes. Gene therapy approaches hold promise for treating primary CoQ10 deficiencies, and combination therapies with compounds such as PQQ, selenium, and omega-3 fatty acids may provide synergistic benefits. Additionally, mitochondrial-targeted forms, including MitoQ, are being investigated to deliver CoQ10 directly to the mitochondria, maximizing its therapeutic potential.

5. Conclusion

Coenzyme Q10 is a vital component of mitochondrial function, playing a central role in energy metabolism, redox balance, and the maintenance of membrane stability. Extensive preclinical research has demonstrated its broad biological effects, supporting cardiovascular protection through improved myocardial energy efficiency and reduced oxidative stress, neuroprotection by preserving neuronal mitochondrial function and limiting protein aggregation, and metabolic regulation via enhanced mitochondrial biogenesis and insulin sensitivity. Additionally, CoQ10 contributes to renal and hepatic protection by mitigating mitochondrial damage and inflammation, enhances fertility by improving gamete mitochondrial function, and exerts potent antioxidant and anti-inflammatory activities. These multifaceted actions provide a strong mechanistic rationale for their investigation across a wide range of disease contexts and therapeutic applications. Clinical evidence for CoQ10 is most robust in cardiovascular and metabolic contexts. It is particularly well-supported for heart failure, as demonstrated by the Q-SYMBIO trial, as well as for hypertension and statin-induced myopathy. Additional areas with meaningful clinical support include migraine prophylaxis, adjunctive therapy in type 2 diabetes, improvement of male and female fertility, and mitigation of aging-related oxidative decline. These findings highlight CoQ10's therapeutic versatility across multiple organ systems and disease states. Future research using enhanced delivery systems may unlock fuller therapeutic potential, especially in neurological and genetic mitochondrial disorders.

Compliance with ethical standards

Disclosure of conflict of interest

The authors have no conflict of interest

References

[1] Alam, M. A., & Rahman, M. M. (2014). Mitochondrial oxidative stress and Coenzyme Q10. Clinical Nutrition, 33(3), 482–490.

[2] Al-Megrin, W. A., Soliman, D., Kassab, R. B., Metwally, D. M., & Amin, H. K. (2020). Coenzyme Q10 protects against oxidative stress and inflammation in experimental models. Molecular Biology Reports, 47(9), 6849–6861.

[3] Bagheri, A., Rashno, M., Keshavarz, M., & Akbari, A. (2023). Therapeutic potential of Coenzyme Q10 in neurodegenerative disorders. Neurochemical Research, 48(4), 1120–1136.

[4] Barcelos, I. P., & Navas, P. (2019). Coenzyme Q and the regulation of mitochondrial metabolism. Molecular Aspects of Medicine, 69, 1–16.

[5] Beal, M. F., Matthews, R. T., Tieleman, A., & Shults, C. W. (1998). Coenzyme Q10 attenuates mitochondrial dysfunction in neurodegeneration. Annals of Neurology, 44(5), 719–723.

[6] Bentinger, M., Tekle, M., & Dallner, G. (2010). Coenzyme Q — biosynthesis and functions. Biochemical and Biophysical Research Communications, 396, 74–79

[7] Boroujeni, M. B., Salehi, I., & Mohammadi, M.(2017). Neuroprotective effects of Coenzyme Q10 against oxidative stress. Metabolic Brain Disease, 32(4), 1191–1203.

[8] Castro-Marrero, J., Cordero, M. D., Sáez-Francàs, N., Jimenez-Gutierrez, C., Aguilar-Morante, D., Aliste, L., Alegre, J., & Sánchez-Alcázar, J. A. (2021). Therapeutic role of Coenzyme Q10.Antioxidants, 10(4), 654.

[9] Chen, Y., Lee, S., & Chen, J. (2019). Coenzyme Q10 in inflammation and oxidative stress. International Journal of Molecular Sciences, 20(19), 4724.

[10] Chen, Z., Li, Y., & Wang, Y. (2018). Coenzyme Q10 and redox signaling. Journal of Cellular Biochemistry, 119(6), 4779–4788.

[11] Dludla, P. V., Nkambule, B. B., & Mazibuko-Mbeje, S. E. (2020). Coenzyme Q10 as a metabolic and antioxidant modulator. Oxidative Medicine and Cellular Longevity, 2020, 6863248.

[12] Engelsen, J., Nielsen, J. D., & Hansen, K. F. (2003). [Effect of coenzyme Q10 and Ginkgo biloba on warfarin dosage in patients on long-term warfarin treatment: A randomized, double-blind, placebo-controlled cross-over trial]. Ugeskrift for Læger, 165(18), 1868–1871.

[13] Enríquez, J. A., Fernández-Silva, P., Montoya, J., & López-Pérez, M. J. (2014). Mitochondrial respiratory chain and human disease. Current Opinion in Genetics & Development, 26, 45–52.

[14] Evans, M., Rees, A., & Smith, A. (2009). Effects of Coenzyme Q10 on oxidative stress and muscle metabolism. Current Therapeutic Research, 70 (2), 134–146.

[15] Fakharaldeen, S. A., Althobaiti, Y. S., & Almeer, R. S. (2023). Coenzyme Q10 attenuates inflammation and oxidative stress. Biomedicine & Pharmacotherapy, 158, 114144.

[16] Fiorenza, M., Gunnarsson, T. P., Hostrup, M., Iaia, F. M., Schena, F., Pilegaard, H., & Bangsbo, J. (2023). Metabolic stress, mitochondrial adaptations, and the role of Coenzyme Q10 in skeletal muscle performance. Redox Biology, 58, 102548

[17] Fischer, A., Niklowitz, P., Menke, T., & Döring, F. (2014), Promotion of growth by Coenzyme Q10 is linked to gene expression in Caenorhabditis elegans. Biochemical and Biophysical Research Communications, 452, 920–927.

[18] Flourou, S., Gkikas, I., Bouris, D., & Papageorgiou, C. (2020). Mitochondrial dysfunction and Coenzyme Q10 deficiency in fatigue-related disorders. Mitochondrion, 52, 77–85.

[19] Fratter, C., Hargreaves, I., Mantle, D., & Heales, S. (2025). Primary and secondary Coenzyme Q10 deficiencies: Diagnosis and management. Journal of Inherited Metabolic Disease, 48(1), 45–60.

[20] González-García, P., Hidalgo-Gutiérrez, A., & Navas, P. (2021). Coenzyme Q and mitochondrial redox homeostasis. Antioxidants, 10(9), 1406.

[21] Halder, S., Dutta, A., & Ghosh, A. (2025). Emerging role of Coenzyme Q10 in neurodegenerative diseases. Neurotherapeutics, 22(1), 55–71.

[22] Hernández-Camacho, J. D., García-Corzo, L., Fernández-Ayala, D. J. M., & Navas, P. (2021). Coenzyme Q at the plasma membrane: A gatekeeper of cellular redox homeostasis. Antioxidants, 10(7), 1110

[23] Hernández-Camacho, J. D., García-Corzo, L., Fernández-Ayala, D. J. M., Navas, P., & López-Lluch, G. (2021). Coenzyme Q at the hinge of health and metabolic diseases. Antioxidants, 10(11), 1785.

[24] Holbrook, A. M., Pereira, J. A., Labiris, R., et al. (2005). Systematic overview of warfarin and its drug and food interactions. Archives of Internal Medicine, 165(10), 1095–1106.

[25] Hughes, B. G., Potturi, P., & Jones, D. P. (2021). Redox signaling and mitochondrial dysfunction: Implications for Coenzyme Q10 therapy. Free Radical Biology and Medicine, 172, 287–299.

[26] Lafuente, R., González-Comadrán, M., Solà, I., López, G., Brassesco, M., Carreras, R., & Checa, M. A. (2013). Coenzyme Q10 and male infertility: A meta-analysis. Journal of Assisted Reproduction and Genetics, 30(9), 1147–1156.

[27] Landbo, C., & Almdal, T. P. (1998). Interaction between warfarin and coenzyme Q10. Ugeskrift for Laeger, 160(22), 3226–3227

[28] Lee, B. J., Huang, Y. C., Chen, S. J., & Lin, P. T. (2014). Coenzyme Q10 supplementation reduces oxidative stress and improves antioxidant enzyme activity in patients with coronary artery disease. Nutrition, 30(6), 623–629.

[29] Lenaz, G., & Genova, M. L. (2009). Structural and functional organization of the mitochondrial respiratory chain: A dynamic super-assembly. The International Journal of Biochemistry & Cell Biology, 41(10), 1750–1772.

[30] López-Lluch, G., Rodríguez-Aguilera, J. C., Santos-Ocaña, C., & Navas, P. (2019). Mitochondrial Coenzyme Q: Biosynthesis, functional roles, and medical relevance. Antioxidants, 8(9)

[31] Mahajan, S., Tandon, V., & Sharma, S. (2020). Coenzyme Q10 improves mitochondrial function in metabolic disease. Molecular and Cellular Biochemistry, 470(1–2), 1–12.

[32] Mantle, D. (2020). Coenzyme Q10 and degenerative disorders: Mitochondrial mechanisms and therapeutic potential. BioFactors, 46(2), 203–214.

[33] Mantle, D. (2024). Coenzyme Q10: Clinical applications in mitochondrial and neurodegenerative disorders. Nutrients, 16(2), 245.

[34] Mantle, D., & Dybring, A. (2020). Coenzyme Q10 in clinical medicine: Mitochondrial mechanisms and therapeutic outcomes. BioFactors, 46 (5), 705–718.

[35] Mantle, D., & Hargreaves, I. (2023). Coenzyme Q10 therapy in mitochondrial disease. Mitochondrion, 68, 102–111.

[36] Mantle, D., Cufflin, N., Purcell, S., & Hargreaves, I. (2025). Clinical perspectives of Coenzyme Q10 in neurological and mitochondrial disorders. Nutrients, 17(3), 398.

[37] Mantle, D., et al. (2025). Nutrients, 17, 112.

[38] Marcheggiani, F., Cirilli, I., Orlando, P., Silvestri, S., & Tiano, L. (2019). Coenzyme Q10 supplementation in aging and disease: Molecular mechanisms. Aging Clinical and Experimental Research, 31(6), 785–798.

[39] Miles, M. V., Horn, P. S., Morrison, J. A., Tang, P. H., DeGrauw, A. J., & Pesce, A. J. (2007). Plasma Coenzyme Q10 reference intervals and biological variation. Clinical Chimica Acta, 386 (1–2), 33–38.

[40] Millichap, J. J., Stack, C. V., & Wirrell, E. C. (2024). Mitochondrial dysfunction and Coenzyme Q10 deficiency in epilepsy. Epilepsy Research, 196, 107136.

[41] Moon, Y., Lee, K., & Park, S. (2005). Neuroprotective effects of Coenzyme Q10. Brain Research, 1052(1), 1–8.

[42] Neergheen, V. S. (2017). Coenzyme Q10 as a mitochondrial bioenergetic and antioxidant agent: Implications for human health. Mitochondrion, 34, 135–150.

[43] Nolfi-Donegan, D., Braganza, A., & Shiva, S. (2020). Mitochondrial electron transport: Oxidative phosphorylation and beyond. Redox Biology, 37, 101674

[44] Papucci, L., Schiavone, N., Witort, E., Donnini, M., Lapucci, A., Tempestini, A., Formigli, L., Zecchi-Orlandini, S., & Orlandini, G. (2003). Coenzyme Q10 prevents apoptosis by inhibiting mitochondrial depolarization independently of its antioxidant property. Journal of Biological Chemistry, 278(30), 28220–28228.

[45] Paradies, G., Paradies, V., & Ruggiero, F. M. (2014). Role of cardiolipin and Coenzyme Q in mitochondrial dysfunction. Biochimica et Biophysica Acta (BBA) – Bioenergetics, 1837(4), 408–417.

[46] Pastor-Maldonado, C. J., Suárez-Rivero, J. M., Povea-Cabello, S., Álvarez-Córdoba, M., Villalón-García, I., Munuera-Cabeza, M., & Sánchez-Alcázar, J. A. (2020). Coenzyme Q deficiency induces mitochondrial dysfunction and oxidative stress. Redox Biology, 34, 101538

[47] Rizzardi, A. E., Johnson, A. T., & Vogel, R. I. (2021). Mitochondrial oxidative stress and therapeutic role of Coenzyme Q10. Redox Biology, 42, 101875.

[48] Rodríguez-Hernández, A., Cordero, M. D., Salviati, L., Artuch, R., Pineda, M., Briones, P., Gómez Izquierdo, L., Cotán, D., Navas, P., & Sánchez-Alcázar, J. A. (2009).

[49] Seidl, S. E., & Potashkin, J. A. (2011). The promise of Coenzyme Q10 in neurodegenerative disease. CNS Neuroscience & Therapeutics, 17(5), 378–391.

[50] Seychell, L., Mantle, D., & Hargreaves, I. (2025). Advances in Coenzyme Q10 therapy for mitochondrial disorders. Mitochondrion, 72, 101–112.

[51] Sharma, S., Kheradpezhouh, E., & Chandrasekaran, K. (2006). Coenzyme Q10 reduces oxidative damage in brain mitochondria. Neuroscience Letters, 401(1–2), 15–19.

[52] Sherer, T. B., Betarbet, R., & Greenamyre, J. T. (2003). Environment, mitochondria, and Parkinson's disease. Neuroscientist, 9(2), 91–100.

[53] Sikorska, M., Lanthier, P., & Sandhu, J. K. (2014). Neuroprotective effects of Coenzyme Q10. Molecular Neurobiology, 49(2), 984–994.

[54] Sohet, F. M., Neyrinck, A. M., & Delzenne, N. M. (2009). Coenzyme Q10 and metabolic regulation. British Journal of Nutrition, 102(9), 1391–1399.

[55] Sood, A., Mahajan, R., & Sharma, S. (2024). Therapeutic potential of Coenzyme Q10 in fatigue, aging, and mitochondrial disorders. Nutrients, 16(3), 412.

[56] Staiano, L., De Matteis, A., & Tiano, L. (2023). Cellular functions of Coenzyme Q10. Cells, 12(8), 1094.

[57] Suárez-Rivero, J. M., Pastor-Maldonado, C. J., de la Cruz-Ojeda, P., Povea-Cabello, S., Álvarez-Córdoba, M., Villalón-García, I., & Sánchez-Alcázar, J. A. (2019). Coenzyme Q10 deficiency and mitochondrial dynamics. Antioxidants, 8(11), 497.

[58] Suárez-Rivero, J. M., Pastor-Maldonado, C. J., Povea-Cabello, S., Álvarez-Córdoba, M., Villalón-García, I., Munuera-Cabeza, M., Suárez-Carrillo, A., … & Sánchez-Alcázar, J. A. (2021). Coenzyme Q10 analogues: Benefits and challenges for therapeutics. Antioxidants, 10(2), 236.

[59] Suárez-Rivero, J. M., Villanueva-Paz, M., de la Cruz-Ojeda, P., de la Mata, M., Cotán, D., Oropesa-Ávila, M., & Sánchez-Alcázar, J. A. (2021). Mitochondrial dynamics and Coenzyme Q10 deficiency. Antioxidants, 10(2), 321

[60] Tsai, K. L., Chen, L. H., Chiou, S. H., & Tsai, C. S. (2012). Coenzyme Q10 suppresses oxidative stress and improves mitochondrial function. Neurobiology of Aging, 33(7), 1590–1601.

[61] Tsuneki, H., Sekizaki, N., Suzuki, T., Kobayashi, S., & Wada, T. (2013). Coenzyme Q10 prevents mitochondrial dysfunction in metabolic disorders. Diabetes, 62(7), 2359–2370.

[62] Umer, M., Khan, M. S., & Rahman, A. U. (2025). Coenzyme Q10 and mitochondrial neuroprotection. Neuroscience Research, 190, 18–29.

[63] Wen, Y., Li, X., Zhang, Y., & Liu, J. (2025). Emerging roles of Coenzyme Q10 in mitochondrial signaling and disease modulation. Free Radical Biology and Medicine, 198, 120–132.

[64] Xie et al., 2020; Chen et al., 2024, Coenzyme Q10 for Enhancing Physical Activity and Extending the Human Life Cycle.

[65] Xu, Y., Guan, Y., Xu, J., & Wang, H. (2018). Coenzyme Q10 supplementation improves mitochondrial function and oxidative stress in metabolic disease models.Journal of Nutritional Biochemistry, 57, 155–164.

[66] Xu, Y., Li, J., & Chen, S. (2017). Coenzyme Q10 and mitochondrial bioenergetics. Biochimica et Biophysica Acta (BBA) – Bioenergetics, 1858(6), 556–567

[67] Yang, X., Zhang, Y., & Xu, H. (2009). Mitochondrial protection by Coenzyme Q10. Journal of Neurochemistry, 109(5), 1427–1439.

[68] Yuan, X., Wang, Y., & Li, H. (2023). Coenzyme Q10 modulates mitochondrial bioenergetics and redox signaling. Free Radical Biology and Medicine, 201, 112–124.

[69] Zaki, M. H., & Burt, B. M. (2016). Coenzyme Q10 and mitochondrial redox signaling. Free Radical Biology and Medicine, 100, 225–235.

[70] Zhang, M., Wang, L., & Chen, Y. (2018). Mitochondrial protection by Coenzyme Q10 under oxidative stress conditions. Oxidative Medicine and Cellular Longevity, 2018, 8921743.

[71] Zhang, Y., Aberg, F., Appelkvist, E. L., Dallner, G., & Ernster, L. (2017). Ubiquinone synthesis, regulation, and its role in mitochondrial function.Biochimica et Biophysica Acta (BBA) – Bioenergetics, 1858 (7), 793–803.

[72] Zhang, Y., Wang, S., & Li, X. (2019). Coenzyme Q10 reduces oxidative stress in cellular models. Oxidative Medicine and Cellular Longevity, 2019, 8036197.

[73] Zhao, Q., Li, H., Chang, L., & Li, Y. (2022). Coenzyme Q10 supplementation improves mitochondrial function and reduces oxidative damage. Frontiers in Pharmacology, 13, 857932.