LiposoMax™ Liposomal CoQ10® has enhance antioxidant activity and supports cellular oxidative phosphorylation.

Pedro Perez, Ph.D., Kevin Perez and Benjamin S. Weeks, Ph.D.

Abstract

CoQ10 is a valuable ergogenic supplement which serves as a cofactor for mitochondrial enzymes where it transfers electrons between complexes of the electron transport chain in the synthesis of ATP. Consequently, CoQ10 is also vital in protecting cells from the oxidative stress that results from loss of electrons (oxidation) during ATP production. CoQ10 can also localize in cellular membranes and directly scavenge xenobiotic derived oxidants. In human subjects, CoQ10 supplementation increases plasma and cellular levels of CoQ10. Further, clinical studies have shown that CoQ10 supplementation can improve neurological and cardiovascular outcomes and reduce inflammation in patients with COPD, Covid19, congestive heart failure and diabetes. CoQ10 has been incorporated into liposomes to enhance absorption and cellular distribution and indeed liposomal CoQ10 is better absorbed and provides better protection from oxidative stress. Here we show that Liposomax™ Liposomal CoQ10® demonstrates enhanced increased protection of neurons from oxidative stress. We also show enhanced neurite outgrowth which is associated with bursts of oxidative phosphorylation and ATP synthesis.

Introduction

CoQ10, also known as ubiquinol (reduced) or ubiquinone (oxidized), is a vitamin-like cofactor that both supports mitochondrial enzyme activity in the production of ATP and supports antioxidant activity by scavenging reactive oxidant species (ROS) (1, 2). CoQ10 is considered vitamin-like because it is both an enzyme cofactor and a free radical scavenger but unlike vitamins, the human body synthesizes CoQ10 primarily in the liver (1, 2). While we make our own, CoQ10 is also acquired from the diet and as its name suggests it is ubiquitous and widely available in a variety of foods including some meats, vegetables and nuts (1 – 3). It can also be important to supplement CoQ10 to boost levels in the body. Indeed, oral supplementation with CoQ10 increases plasma and cellular levels of CoQ10 (3- 5) and is a supplement of great interest for its health benefits (6).

Published clinical studies show that CoQ10 supplementation can help to address a wide range of human disease conditions. For example, in cases of genetic deficiencies in the enzymes of CoQ10 biosynthesis, patients experience nervous system and muscular difficulties including cognitive dysfunction, seizures and muscular hypotonia and dystonia which can be improved with CoQ10 supplementation (7). CoQ10 supplementation can also reduce inflammation and disease complications in patients with congestive heart failure, COPD and CoVid19 (8 – 10). CoQ10 supplementation also increases insulin sensitivity and improves cardiovascular function in patients with diabetes (11). CoQ10 supplementation can also improve patient outcomes post stroke and poste heart and vascular surgeries (9). While CoQ10 supplementation can address these deficiencies and diseases, a great deal of interest also surrounds the benefits of CoQ10 supplementation as an ergogenic factor in states of normal and heightened physiological activity. Specifically, in human clinical trials, the ergogenic properties of CoQ10 have proven to be both antiaging and to boost athletic performance (5, 12 – 18)

Mitochondria are the powerhouse of the cell producing ATP with is the chemical currency for muscle and nerve activity all anabolic enzymes. CoQ10 supplementation can directly boost the availability of ATP for muscle action and repair (6). Muscles undergo damage during exercise due to the oxidative stress involved in ATP synthesis and depletion. In clinical studies, athletes taking oral CoQ10 supplements have experienced less muscle damage and reduced cellular ROS accumulation during exercise and improved muscle repair post-exercise (14, 19 – 22). Interestingly, CoQ10 can also improve the performance in older and aged athletes (23).

Aging involves reduced mitochondrial function and accumulated oxidative stress. Aging is also associated with a reduced ability of the body to synthesize CoQ10. Consequently, CoQ10 supplementation is of great interest to not only the older athlete but as an antiaging supplement in general. For example, in clinical studies CoQ10 supplementation reduces the expression of inflammatory markers and markers of aging such as endothelial cell ICAM1, adiponectin, SCF and OPG (24) and also stabilized leukocyte telomere length (25).

The cellular absorption of CoQ10 has been shown to be enhanced by incorporation into liposomes (26, 27). Liposomal CoQ10 has been show to improve pancreatic beta cell survival (28), shows enhanced protection from copper induced oxidative stress (29) reduced neuroinflammation (30) and shows enhanced protection from myocardial infarction (31) and propionic acid induced hepatic inflammation and fibrosis (32) Here we show that Liposomax™ Liposomal CoQ10 enters cells more quickly and is statistically significantly better at both enhanced protection of neuronal of cells from H2O2 induced oxidative stress and enhanced neurite outgrowth than non-liposomal CoQ10.

Materials and Methods

N38 Cell Culture and MTT assay: Murine hypothalamic N38 cells were cultured in DMEM containing 5% heat inactivated fetal Bovine serum (FBS) supplemented with Penn/Strep. For MTT assay, cells were harvested with trypsin-EDTA which was neutralized by medium. The cells were then washed free of serum using DMEM and the cells were resuspended in serum-free DMEM containing and ITS supplement (insulin, selenium and transferrin) (defined medium). The cells were seeded into 24 well plates in 0.5 ml defined medium at $5x10^5$ cells per well and either untreated (control) or treated with 300 μM H2O2 for 24 hours. Cell receiving H2O2 were also concomitantly treated with nonliposomal CoQ10 (NL CoQ10) or LiposoMax™ Liposomal CoQ10® (LiposoMax™ LipoCoQ10) at 0.5 μM, 5 μM, and 50 μM. After 24 hours of treatment, the medium was gently removed and 0.05 mg/ml of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide in 200 μl of phosphate buffered saline (PBS) was added to each well for four hours and incubated at 37ºC. After 4 hours, 300 μl of dimethyl sulfoxide (DMSO) was added to each well and the plate was gently rocked on a shaker at 150 rpm for 10 minutes after which the medium (PBS and DMSO) was collected and clarified by centrifugation and 100 μl of the solution was transferred to duplicate wells of a 96 well plate and the optical density was measured at 570 nm. To determine the percent viability, the OD at 570 was compared to a standard curve of cell number and the cell number correlating to the OD was divided then by the total cell number and multiplied by 100 to give percent viability.

PC12 cell culture and neurite outgrowth: Rat pheochromocytoma PC12 neuronal cells were cultured in DMEM containing 7.5% heat inactivated FBS and 7.5% heat inactivated equine serum supplemented with Penn/Strep. PC12 cells were harvested by agitation and suspended at 2x104 cells/ml of medium containing 50 ng/ml nerve growth factor (NGF) and seeded at $2x10^4$ cells per well in triplicate wells of a 24 well tissue cluster plate. Cells were then either untreated or treated with 50 μM nonliposomal or Liposomax™ Liposomal CoQ10 and incubated in a water-jacketed CO2 incubator at 37oC for 6 hours and photographed at 640X total magnification. The percentage of cells exhibiting neurites was determined by visual inspection by examining 100 cells in each well treatment and determining the number which had neurites at least one time the cell diameter.

Results and Discussion

Liposomax™ Liposomal CoQ10 protects N38 cells from H2O2 toxicity better than non-liposomal CoQ10 (Figure 1). Twenty-four-hour treatment of N38 cells lead to an approximate 60 percent reduction in cell viability. However, both 5 and 50 μM CoQ10 treatment significantly reduced H2O2 toxicity with approximately 70% survival when treated with 50 mM Liposomax™ Liposomal CoQ10 (Figure 1). Liposomax™ Liposomal CoQ10 was statistically significantly better than nonliposomal CoQ10 at protecting N38 cells from H2O2 induced oxidative stress at both 5.0 μM and 50 μM (Figure 1).

Figure 1. Liposomax™ Liposomal CoQ10 provides enhanced protection to neurons from H2O2 induced oxidative stress.

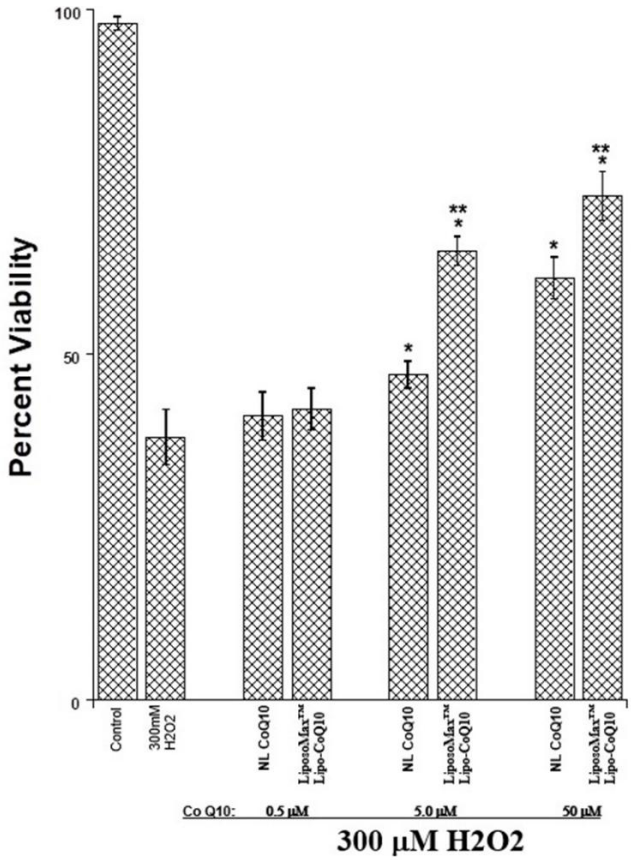

Figure 1. Liposomax™ Liposomal CoQ10 provides enhanced protection to neurons from H2O2 induced oxidative stress. Murine Hypothalamic N38 cells were seeded into 24 well plates in 0.5 ml serum-free DMEM supplemented with insulin, selenium and transferrin (defined medium) at $5x10^5$ cells per well and either untreated (control) or treated with 300 μM H2O2 for 24 hours. Cell receiving H2O2 were also concomitantly treated with nonliposomal CoQ10 (NL CoQ10) or LiposoMax™ Liposomal CoQ10® (LiposoMax™ LipoCoQ10) at 0.5 μM, 5 μM, and 50 μM. After 24 hours of treatment, the medium was gently removed and 0.05 mg/ml of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide in 200 μl of phosphate buffered saline was added to each well for four hours and incubated at 37°C. After 4 hours, 300 μl of dimethyl sulfoxide (DMSO) was added to each well and the plate was gently rocked on a shaker at 150 rpm for 10 minutes after which the medium (PBS and DMSO) was collected and clarified by centrifugation and 100 μl of the solution was transferred to duplicate wells of a 96 well plate and the optical density was measured at 570 nm. To determine the percent viability, the OD at 570

was compared to a standard curve of cell number and the cell number correlating to the OD was divided then by the total cell number and multiplied by 100 to give percent viability.

Liposomax™ Liposomal CoQ10 stimulates neurite outgrowth in PC12 cells more rapidly than nonliposomal CoQ10. Figure 2A shows photomicrographs of PC12 cells 6 hours after NGF treatment. Maximal neurite outgrowth is achieved after 72 hours and is not shown. Therefore, the enhanced neurite outgrowth shown here represents a more rapid stimulation at an early timepoint. Figure 2B shows the percentage of cells with neurites at six hours post NGF treatment. Both nonliposomal and Liposomax™ Liposomal CoQ10 enhance neurite outgrowth however Liposomax™ Liposomal CoQ10 is statistically significantly better than non-liposomal CoQ10 (Figure 2B).

Figure 2. Liposomax™ Liposomal CoQ10 enhances CoQ10 neurite promoting activity.

Figure 2A

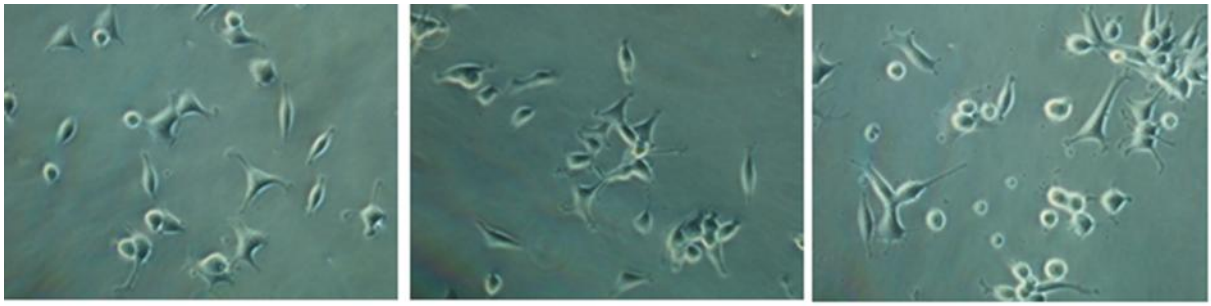

Figure 2B

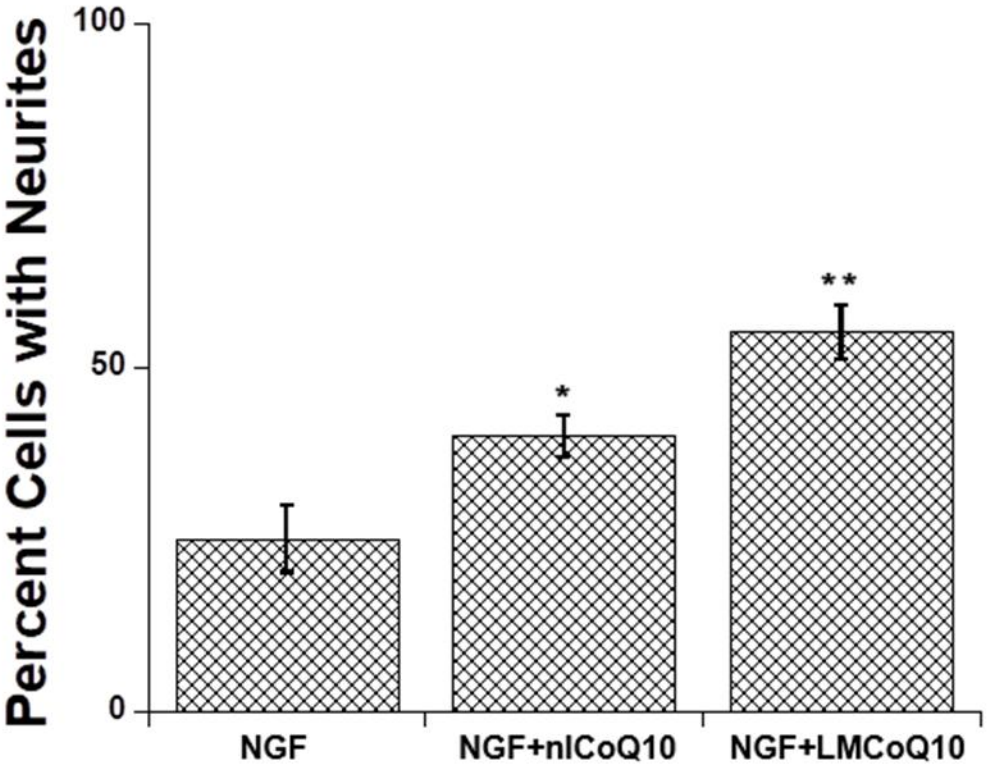

Figure 2. Liposomax™ Liposomal CoQ10 enhances CoQ10 neurite promoting activity. In figure 2A above PC12 cells were cultured with NGF alone (left panel) or NGF with 50 μM nonliposomal CoQ10 (middle panel) or 50 μM Liposomax™ Liposomal CoQ10 (right panel) and incubated for six hours and photographed at 540X total magnification. Figure 2B shows the same results when the percentage of cells exhibiting neurites is counted. The single asterisk shows that nonliposomal CoQ10 (nlCoQ10) stipulates neurite outgrowth in PC12 cells beyond NGF alone. The double asterisk shows that Liposomax liposomal CoQ10 (LMCoQ10) is statistically significantly extent in an analysis of variance more effective at enhancing neurite outgrowth than the nonliposomal form.

Discussion and Conclusions

Taken together these data show that Liposomax™ Liposomal CoQ10 is better absorbed into cellular mitochondrial compartments where it can better protect cells from oxidative stress. Further, these data are unique in that they show that CoQ10 and in the Liposomax™ Liposomal CoQ10 form enhance cellular ATP production to meet the high demand of neuronal cells during neurite outgrowth.

More importantly, these data show that Liposomax™ Liposomal CoQ10 has faster and greater beneficial effects on these parameters when compared to no liposomal form, which explains the Liposomax™ Liposomal CoQ10 improved bioactivity. Here we present a new delivery form, LiposoMax™ Liposomal CoQ10® which is more active and effective than non-liposomal CoQ10 with regard to stimulation of neurite outgrowth, protection against oxidative stress, enhance cellular ATP production, promoting healthy mitochondrial function and the protection of the immune system and cardiovascular system from induced inflammatory mechanisms.

LiposoMax™ Liposomal CoQ10® provides an innovative solution to effectively increase cellular CoQ10 and its antioxidant activity. As demonstrated in Figure 1, LiposoMax™ Liposomal CoQ10® statistically significantly enhances cellular protection compared to conventional, non-liposomal CoQ10. Specifically, it outperformed non-liposomal CoQ10 in shielding neuronal cells from oxidative damage induced by hydrogen peroxide. As demonstrated in Figure 2A and 2B, LiposoMax™ Liposomal CoQ10® statistically significantly enhances nerite outgrowth compared to conventional, non-liposomal CoQ10. Specifically, it outperformed non-liposomal CoQ10 in PC12 cells respond to nerve growth factor (NGF) treatment by extending neurites, and significant neurite outgrowth in neuronal cells post-treatment.

The ability of LiposoMax™ Liposomal CoQ10® to quickly affect cell behavior and more rapid response is an indication of its better absorption and better avidity for the cell surface, and peripheral sites and more efficiently intracellular activity, and its improved bioavailability which facilitates faster and more efficient cellular uptake and improved bioactivity and the LiposoMax™ Liposomal CoQ10® statistically significantly outperformed on these parameters when compared to non-liposomal CoQ10.

References

1) Cirilli, Ilenia et al. “Role of Coenzyme Q10 in Health and Disease: An Update on the Last 10 Years (2010-2020).” Antioxidants (Basel, Switzerland) vol. 10,8 1325. 23 Aug. 2021, doi:10.3390/antiox10081325
2) Pelton R. Coenzyme Q10: A Miracle Nutrient Advances in Understanding. Integr Med (Encinitas). 2020;19(2):16-20.
3) Vitetta, Luis et al. “The Plasma Bioavailability of Coenzyme Q10 Absorbed from the Gut and the Oral Mucosa.” Journal of functional biomaterials vol. 9,4 73. 15 Dec. 2018, doi:10.3390/jfb9040073
4) Bhagavan, H. N., & Chopra, R. K. (2006). Coenzyme Q10: Absorption, tissue uptake, metabolism and pharmacokinetics. Free Radical Research, 40(5), 445–453. https://doi.org/10.1080/10715760600617843
5) Jan Aaseth, Jan Alexander, Urban Alehagen, Coenzyme Q10 supplementation – In ageing and disease, Mechanisms of Ageing and Development, Volume 197, 2021, 111521, ISSN 0047-6374, https://doi.org/10.1016/j.mad.2021.111521
6) Drobnic, Franchek et al. “Coenzyme Q10 Supplementation and Its Impact on Exercise and Sport Performance in Humans: A Recovery or a Performance-Enhancing Molecule?.” Nutrients vol. 14,9 1811. 26 Apr. 2022, doi:10.3390/nu14091811
7) Hargreaves, Iain et al. “Disorders of Human Coenzyme Q10 Metabolism: An Overview.” International journal of molecular sciences vol. 21,18 6695. 13 Sep. 2020, doi:10.3390/ijms21186695

8) Qazi SU, Bin Naeem MA, Umar M, et al. Evaluating the efficacy of ubiquinol in heart failure patients: a systematic review and meta-analysis. Future Cardiol. 2024;20(4):221-228. doi:10.1080/14796678.2024.2352308
9) Gutierrez-Mariscal FM, Arenas-de Larriva AP, Limia-Perez L, Romero-Cabrera JL, Yubero-Serrano EM, López-Miranda J. Coenzyme Q10 Supplementation for the Reduction of Oxidative Stress: Clinical Implications in the Treatment of Chronic Diseases. Int J Mol Sci. 2020;21(21):7870. Published 2020 Oct 23. doi:10.3390/ijms21217870
10) Chen LZ, Cai Q, Zheng PF. Mitochondrial metabolic rescue in post-COVID-19 syndrome: MR spectroscopy insights and precision nutritional therapeutics. Front Immunol. 2025;16:1597370. Published 2025 May 23. doi:10.3389/fimmu.2025.1597370
11) Shen, Qiuhua, and Janet D Pierce. "Supplementation of Coenzyme Q10 among Patients with Type 2 Diabetes Mellitus." Healthcare (Basel, Switzerland) vol. 3,2 296-309. 21 May. 2015, doi:10.3390/healthcare3020296
12) Díaz-Casado ME, Quiles JL, Barriocanal-Casado E, et al. The Paradox of Coenzyme Q10 in Aging. Nutrients. 2019;11(9):2221. Published 2019 Sep 14. doi:10.3390/nu11092221
13) Alf, D., Schmidt, M.E. & Siebrecht, S.C. Ubiquinol supplementation enhances peak power production in trained athletes: a double-blind, placebo controlled study. J Int Soc Sports Nutr 10, 24 (2013). https://doi.org/10.1186/1550-2783-10-24
14) Orlando P, Silvestri S, Galeazzi R, et al. Effect of ubiquinol supplementation on biochemical and oxidative stress indexes after intense exercise in young athletes. Redox Rep. 2018;23(1):136-145. doi:10.1080/13510002.2018.1472924
15) Qu H, Qu Y. Can coenzyme Q10 supplementation reduce exercise-induced muscle damage and oxidative stress in athletes? A systematic review and meta-analysis. Complement Ther Clin Pract. Published online May 8, 2025. doi:10.1016/j.ctcp.2025.102001
16) Bian Z, Wei L. The role of coenzyme Q10 in exercise tolerance and muscle strength. Arch Physiol Biochem. Published online May 24, 2025. doi:10.1080/13813455.2025.2507746
17) Sarmiento A, Diaz-Castro J, Pulido-Moran M, Kajarabille N, Guisado R, Ochoa JJ. Coenzyme Q10 Supplementation and Exercise in Healthy Humans: A Systematic Review. Curr Drug Metab. 2016;17(4):345-358. doi:10.2174/1389200216666151103115654
18) Mason SA, Trewin AJ, Parker L, Wadley GD. Antioxidant supplements and endurance exercise: Current evidence and mechanistic insights. Redox Biol. 2020;35:101471. doi:10.1016/j.redox.2020.101471.
19) Kon M, Tanabe K, Akimoto T, et al. Reducing exercise-induced muscular injury in kendo athletes with supplementation of coenzyme Q10. Br J Nutr. 2008;100(4):903-909. doi:10.1017/S0007114508926544
20) Ovchinnikov AN, Paoli A, Seleznev VV, Deryugina AV. Royal jelly plus coenzyme Q10 supplementation improves high-intensity interval exercise performance via changes in plasmatic and salivary biomarkers of oxidative stress and muscle damage in swimmers: a randomized, double-blind, placebo-controlled pilot trial. J Int Soc Sports Nutr. 2022;19(1):239-257. Published 2022 Jun 16. doi:10.1080/15502783.2022.2086015
21) Hui Qu, Yueyao Qu, Can coenzyme Q10 supplementation reduce exercise-induced muscle damage and oxidative stress in athletes? A systematic review and meta-analysis, Complementary Therapies in Clinical Practice, Volume 60, 2025, 102001, ISSN 1744-3881, https://doi.org/10.1016/j.ctcp.2025.102001.
22) Phyo Pyae Thar, Teerarat Likitwattanasade, Ratchakrit Srikuea, Post-workout supplementation with CoQ10 and sports drink on exercise performance and muscle recovery after exercise in normal and overweight males, Sports Medicine and Health Science, 2025, ISSN 2666-3376, https://doi.org/10.1016/j.smhs.2025.02.005.
23) Deichmann RE, Lavie CJ, Dornelles AC. Impact of coenzyme Q-10 on parameters of cardiorespiratory fitness and muscle performance in older athletes taking statins. Phys Sportsmed. 2012;40(4):88-95. doi:10.3810/psm.2012.11.1991
24) Alehagen U, Alexander J, Aaseth JO, Larsson A, Svensson E, Opstad TB. Effects of an Intervention with Selenium and Coenzyme Q10 on Five Selected Age-Related Biomarkers in Elderly Swedes Low in

Selenium: Results That Point to an Anti-Ageing Effect-A Sub-Analysis of a Previous Prospective Double-Blind Placebo-Controlled Randomised Clinical Trial. Cells. 2023;12(13):1773. Published 2023 Jul 4. doi:10.3390/cells12131773

25) Opstad TB, Alexander J, Aaseth JO, Larsson A, Seljeflot I, Alehagen U. Selenium and Coenzyme Q10 Intervention Prevents Telomere Attrition, with Association to Reduced Cardiovascular Mortality-Sub-Study of a Randomized Clinical Trial. Nutrients. 2022;14(16):3346. Published 2022 Aug 15. doi:10.3390/nu14163346
26) Maciejewska-Stupska K, Czarnecka K, Szymański P. Bioavailability enhancement of coenzyme Q10: An update of novel approaches. Arch Pharm (Weinheim). 2024;357(8):e2300676. doi:10.1002/ardp.202300676
27) Li X, Zhao X, Wang J, Xu B, Feng J, Huang W. High-Pressure Microfluidic Homogenization Improves the Stability and Antioxidant Properties of Coenzyme Q10 Nanoliposomes. Biology (Basel). 2025;14(5):568. Published 2025 May 19. doi:10.3390/biology14050568
28) Xiao S, Rao L, Yan C, et al. Aptamer Functionalized Liposomes Co-Loaded with Exenatide-4 and Coenzyme Q10 Ameliorate Type 2 Diabetes Mellitus by Improving Pancreatic β Cell Function. Int J Nanomedicine. 2025;20:3363-3378. Published 2025 Mar 17. doi:10.2147/IJN.S510240
29) Alghibiwi HK, Alhusiani AM, Sarawi WS, et al. Coenzyme Q10 and its liposomal form prevent copper cardiotoxicity by attenuating oxidative stress, TLR-4/NF-κB signaling and necroptosis in rats. Cell Mol Biol (Noisy-le-grand). 2025;71(1):118-124. Published 2025 Feb 2. doi:10.14715/cmb/2025.70.1.13
30) Umer H, Sharif A, Khan HM, et al. Mitigation of Neuroinflammation and Oxidative Stress in Rotenone-Induced Parkinson Mouse Model through Liposomal Coenzyme-Q10 Intervention: A Comprehensive In-vivo Study. Inflammation. Published online January 21, 2025. doi:10.1007/s10753-025-02237-0
31) Lei W, Yang J, Wang J, et al. Synergetic EGCG and coenzyme Q10 DSPC liposome nanoparticles protect against myocardial infarction. Biomater Sci. 2023;11(20):6862-6870. Published 2023 Oct 10. doi:10.1039/d3bm00857f
32) Alhusaini AM, Alsoghayer R, Alhushan L, Alanazi AM, Hasan IH. Acetyl-L-Carnitine and Liposomal Co-Enzyme Q10 Attenuate Hepatic Inflammation, Apoptosis, and Fibrosis Induced by Propionic Acid. Int J Mol Sci. 2023;24(14):11519. Published 2023 Jul 15. doi:10.3390/ijms241411519