Ubiquinol is superior to ubiquinone to enhance Coenzyme Q10 status in older men

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Abstract Coenzyme Q10 (CoQ10) exerts its functions in the body through the ability of its benzoquinone head group to accept and donate electrons. The primary functions are to relay electrons for the ATP production in the electron transport chain and to act as an important lipophilic antioxidant. Ubiquinone, the oxidized form of CoQ10, is commonly formulated in commercial supplements, and it must be reduced to ubiquinol to exert CoQ10's functions after consumption. Thus, we aimed to examine whether as compared to ubiquinone, ubiquinol would be more effective to enhance CoQ10 status in older men. We conducted a double-blind, randomized, crossover trial with two 2-week intervention phases and a 2-week washout between crossover. Ten eligible older men were randomized to consume with one of the main meals either ubiquinol or ubiquinone supplement at the dose of 200 mg/d. A total of 4 blood samples were collected after an overnight fast for the determination of ubiquinone and ubiquinol in plasma and PBMC and the assessment of FRAP, total thiol, and malondialdehyde (MDA) in plasma and ATP in PBMC. After 2 weeks of the supplementation, the ubiquinol supplement significantly increased plasma ubiquinone by 1.7 fold from 0.2 to 0.6 µmol/L and total CoQ10 (the sum of 2 forms) by 1.5 fold from 1.3 to 3.4 µmol/L ($p < 0.05$) and tended to increase plasma ubiquinol status by 1.5 fold from 1.1 to 2.8 µmol/L, but did not alter the ratio of ubiquinol to total CoQ10. The ubiquinone supplement insignificantly increases plasma ubiquinol, ubiquinone, and total CoQ10 and did not affect the ratio. Of 10 subjects, six were more responsive to the ubiquinol supplement and 2 were more so to the ubiquinone. The supplementation of both CoQ10 forms did not alter CoQ10 status in PBMC. FRAP, total thiol, MDA in plasma and ATP in PBMC were not changed during the intervention. The significant increase in plasma CoQ10 status observed after the 2-week supplementation suggested that ubiquinol appeared to be a better supplemental form to enhance the CoQ10 status than ubiquinone in older men. Neither ubiquinol nor ubiquinone supplement affected the measured biomarkers of oxidative stress.

Introduction

Coenzyme Q10 (CoQ10) is a lipophilic molecule ubiquitous in all cell membranes and lipoproteins and exists in both reduced and oxidized states, namely ubiquinol and ubiquinone, respectively.[1] CoQ10 can be synthesized in the body with the benzoquinone structure derived from either tyrosine or phenylalanine and an isoprene side chain from acetyl-CoA via the mevalonate pathway.[2] CoQ10 exerts 2 main functions through the ability of its benzoquinone head group to engage in a continuous redox cycle, mainly relaying electrons for the ATP production in the electron transport chain and acting as a lipophilic antioxidant by protecting polyunsaturated fatty acids, proteins, and DNA against oxidation.[3,4] Furthermore, CoQ10 regulates physicochemical properties of membranes and maintains endothelial function.[1]

CoQ10 deficiency is very rare because its status is well maintained primarily through the endogenous biosynthesis.[2,5] Nevertheless, some pathophysiological conditions and medications lead to a less optimal CoQ10 status. For example, its level is declined gradually with age in a number of organs, such as heart and brain, probably ascribed to increased utilization, decreased synthesis or both. [6] Aging is associated with increased production of free radicals and compromised antioxidant defences, leading to the accumulation of deleterious effects of free radicals and sequelae, e.g. cancers, cardiometabolic diseases, and cognitive decline/dementia. Thus, CoQ10 as an important antioxidant may protect against age-related symptoms and diseases. However, dietary sources alone, which in general provide <3 mg/serving, is inadequate to elevate CoQ10 levels to the population average of 1 µg/mL (1.16 µmol/L).[7] Alternatively, CoQ10 supplementation can be one of convenient, feasible ways to increase CoQ10 status and consequent health promotion and prevention. For example, the data of a recent human study showed 24-week supplementation of 120 mg/d CoQ10 ameliorates multiple CVD risk factors in adults with dyslipidemia including blood pressure, lipid profile, and insulin

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resistance.[8] Furtherly, the results of meta-analysis studies showed that CoQ10 supplementation was beneficial to hypertension, dyslipidemia, and inflammation.[9-12]

Prior to mediating its functions, ingested CoQ10 must be absorbed and delivered to target tissues. The bioavailability of ingested nutrients is markedly influenced by an array of factors, such as physicochemical characteristics, delivery system, and physiological and biochemical status of consumers. Ubiquinone, the most common form in CoQ10 supplements, has a very low bioavailability because of its considerable lipophilicity, crystalline state, and high molecular weight.[13] The inferiority of ubiquinone to ubiquinol in the bioavailability has been demonstrated in a few acute pharmacokinetic trials.[14-16] The information on mechanisms by which bioavailability of ubiquinol is superior to ubiquinone is limited. Failla et al. observed in a cell culture study that a reduced intracellular environment was necessary to facilitate absorption of both CoQ10 in the small intestine and subsequent secretion to the circulation.[17] Thus, we hypothesized that ubiquinol would be more bioavailable than ubiquinone in older adults with a low total antioxidant capacity status and total thiol content. To test this hypothesis, we determined ubiquinol and ubiquinone in plasma and peripheral blood mononuclear cells (PBMC) and biomarker of oxidative stress in plasma.

Materials and methods

Chemicals and reagents

Ficoll-Paque Plus, phosphate buffer saline, bovine serum albumin, dimethyl sulfoxide (DMSO), echinenone, trichloroacetic acid, thiobarbituric acid, sodium acetate, sodium phosphate, ferric chloride ($FeCl_3$), 1,1,3,3-tetraethoxypropane, ubiquinol-10, and ubiquinone-10 were purchased from Sigma–Aldrich (St. Louis, MO, USA). NaOH, propanol, isopropanol, methanol, hexane, and glacial acetic acid were purchased from Thermo-Fisher (Pittsburgh, PA). CellTiter-Glo® Assay was obtained from Promega Co. (Madison, WI), fetal bovine serum from ATCC (Manassas, VA), and X-VIVO™ 10 from Lonza (Basel, Switzerland).

Study design

The trial was a double-blind, randomized, crossover design with 5 study visits, including 1 screening visit and 4 study visits. The duration of the whole trial was 8 weeks, including two 14-day intervention phases and a 2-week washout period between 2 intervention phases. Ten eligible adults were randomized to take either 200 mg/day ubiquinol or 200 mg/day ubiquinone with one of the main meals for 2 weeks. Ubiquinol™ and ubiquinone supplements were generously provided by Kaneka Co (Pasadena, TX). The purity of ubiquinol™ is 99.6%, according to the result of a chromatographic analysis. Other ingredients in the supplements include edible oil, emulsifier, beeswax, lecithin, modified cornstarch, glycerol, carrageenan, and disodium phosphate and encapsulated in 10 oval, dark brown soft capsules. Both ubiquinol and ubiquinone have Self-Affirmed GRAS status ("generally recognized as safe"). All supplements were stored in dark at room temperature until use. Before and after each intervention phase, overnight fasting venous blood was drawn for the collection of PBMC and plasma. All collected samples were processed and then stored at -80°C until analyses.

Subjects

Ten men who were >55 y and had BMI between 25-35 kg/m^2 were recruited for the trial. They had to have both <1000 μmol/L Fe^{2+} plasma total antioxidant capacity determined by Ferric Reducing Antioxidant Power (FRAP) and <400 μmol/L total thiol content in plasma.[18-21] Exclusion criteria included 1) receiving dietary supplements (however, subjects who were willing to refrain from the use of these supplements for 1 month prior to their enrolment and throughout the entire study may be considered eligible); 2) use of medications known to affect lipid metabolism; 3) gain or loss of ⍰5% of body weight in the last 6 month; 4) impaired gastrointestinal, renal, and endocrine functions, diseases, conditions or medications influencing gastrointestinal absorption; 5) active treatment for cancer of any type; 6) vegan; and 7) drink ≤14 servings alcohol per week. Subjects were recruited from the Greater Boston area through the Jean Mayer USDA Human Nutrition Research Centre on Aging (HNRCA) volunteer database. All study conducts were performed after study subjects signed informed consent forms. The protocol was approved by Tufts Health Sciences Institutional Review Board and was registered at clinicaltrial.gov.(certificate number NCT03020680).

Biochemical Analysis

PBMC were isolated from fresh EDTA blood using the density gradient centrifugation method with the Ficoll-Isopague solution, according to the manufacturer's protocol (GE Healthcare Bio-Sciences, Pittsburgh, PA) and then were stored at -80°C in a cryoprotective freezing medium (DMSO/fetal bovine serum/ X-VIVO™ 10: 1/20/70) until analysis.[22]

Ubiquinol and ubiquinone in plasma and PBMC were determined using an HPLC-electrochemical detection (HPLC-ECD) method, according to Tang et al. and Franke et al. with slight modifications.[23,24] The HPLC-ECD system included an ESA model 582 solvent delivery module (ESA Laboratories, Inc., Chelmsford, MA, USA) equipped with a double plunger reciprocating pump and an autosampler (Model 542, ESA, MA, USA), and a CoulArray Model 5600A detector (ESA). The whole system was operated under room temperature. The whole extraction procedure was performed under red light to avoid ubiquinol oxidation. Echinenone (30 μL of 2.5 μmol/L) was added before the addition of 1-propanol to serve the internal standard (IS) to monitor the extraction efficiency. CoQ10 in 300 μL plasma and 400 μL PBMC (cell counts ranged from 2 to 14 million) were extracted using 670 and 570 μL 1-propanol, respectively. After centrifugation, the resulting supernatant (850 μL) was dried under N_2 gas and reconstituted with 300 μL 1-propanol for the HPLC-ECD analysis. CoQ10 was eluted from a Zorbax® reversed-phase SB-C18 column (5 μm, 250 x 4.6 mm, Agilent, Santa Clara, CA), according to the chromatographic condition of Franke et al.[24] The concentration of standards ranged from 0.0625 to 1.0 μmol/L and from 0.016 to 0.5 μmol/L for ubiquinol and ubiquinone, respectively, to construct standard curves for plasma and PBMC. The linearity of the standard curve for ubiquinol and ubiquinone in

plasma was illustrated as y = 4.236x - 0.7826 (r^2 = 0.9996) and y = 4.0863x - 0.0006 (r^2 = 0.9998), respectively. In PBMC, the calibration curve of ubiquinol and ubiquinone was y = 3.4081x - 0.0763 (r^2 = 0.9996) and y = 4.3803x - 0.0161 (r^2=0.9999), respectively (**Supplemental Table 1**). Y represents the peak area ratio of ubiquinol or ubiquinone to IS, and x represents the concentration of spiked ubiquinol or ubiquinone in plasma or PBMC suspensions. Recovery of ubiquinol and ubiquinone was carried out by adding the known amounts of both compounds to plasma or PBMC. The recovery rate of ubiquinol and ubiquinone spiked into plasma ranged from 82.11 to 94.58% and from 81.96 to 89.43% with the RSD >5%, and ubiquinol and ubiquinone added to PBMC ranged from 83.74 to 95.93% and from 79.35% to 88.93% with the RSD > 5%, respectively (**Supplemental Table 1**). The recovery rate was compared to the same concentration of the compound analyzed directly by HPLC-ECD. The intra- and inter-day coefficient of variation (CV) of plasma ubiquinol was 0.9 and 3.1%, plasma ubiquinone was 3.5 and 6.4%, PBMC ubiquinol was 1.7 and 1.6%, and PBMC ubiquinone was 7.3 and 6.5%, respectively.

Plasma MDA was measured by an Agilent 1100 HPLC system (Santa Clara, CA) with a fluorometric detector, according to Behrens and Madère with some modifications.[25] Briefly, 0.1 mL plasma was saponified with 5.5 µL of 10 N NaOH at 60°C for 30 min, followed by the addition of 600 µL of 7.2% trichloroacetic acid. The resulting mixture (400 µL) was then incubated with 0.2 ml of 0.6% thiobarbituric acid in sodium acetate buffer (pH 3.5) and 20 µL of 0.031 M $FeCl_3$ at 95°C for 1 h. The MDA conjugate was eluted on a Varian Microsorb 100-5 C18 column (150 x 4.6 mm, 5 µm, Agilent Technologies Inc, Santa Clara, CA) with a mobile phase of 65% sodium phosphate buffer and 35% methanol at 0.8 mL/min flow rate and monitored at 515/553 nm excitation/emission. MDA concentration was calculated based on a standard curve constructed using an authentic standard, 1,1,3,3-tetraethoxypropane. The intra-day CV was 5.7%. The results are expressed as µmol/L.

ATP in PBMC was determined using a CellTiter-Glo® One Solution Assay kit according to the manufacturer's instructions. The intra-day CV was 6.2%.

Statistical Analysis

All data are expressed as the mean ± standard deviation (SD). A sample size calculation was performed as the study was a pilot trial in nature. An ANOVA analysis was performed to assess the significant differences between ubiquinol and ubiquinone supplements, using PROC MIXED with treatment (ubiquinol vs. ubiquinone), sequence (ubiquinol - ubiquinone vs. ubiquinone - ubiquinol), and period (1 vs. 2) as independent variables and subject being included in the random statement, followed by Tukey HSD post-hoc comparison test. Furthermore, the statistical analysis was performed to test the time factor with sequence and period as the independent variables and subjects as the random effect. All above analyses were performed using SAS 9.4 (SAS Institute, Cary, NC). Correlations between all analytes were analysed using the ggcorrplot package (version 0.1.1.9000) in R. Significance was considered at $P \leq 0.05$ (2-tailed).

Results

All study subjects were recruited in Boston metropolitan area between April 2016 and February 2017. Fifty men were phone screened for their eligibility, 13 of them were invited for an on-site screening, and 12 were enrolled and 10 completed with the full compliance. Two completers were lost to contact. Ten men completed the whole trial were 63.9 ± 2.7 years old and had an average body weight of 89.3 ± 8.1 kg and body mass index of 27.7 ± 2.4 kg/m^2.

The change in the status of CoQ10 in plasma and PMBC was first assessed with the combined data of both CoQ10 supplements. In plasma, ubiquinol was significantly increased by 109% after 2 weeks of the supplementation, ubiquinone by 105%, and the sum (ubiquinol plus ubiquinone) by 108% (**Fig. 1**). The ratio of ubiquinol to the sum was not altered by the supplementation. The change in plasma ubiquinol status of individual participants after the supplementation was presented in **Supplemental Fig 1**. Apparently, 6 subjects were more responsive (>100% increase from the corresponding pre-supplementation value) to ubiquinol and 2 subjects were more so to ubiquinone. Of 10 participants, 4 had the pre-intervention plasma ubiquinol concentration below the population average of 1 µg/mL (1.16 µmol/L)[7]. Both CoQ10 supplements appeared to be effective to elevate their values above the population average, and ubiquinol supplement led to an at least 1-fold elevation in 7 subjects and ubiquinone supplement only in 2 subjects.

Plasma ubiquinol concentration was larger by 40.6% after the ubiquinol supplementation than ubiquinone one but the difference did not reach statistical significance. Plasma ubiquinone and the sum were significantly larger by 102.7 and 48.6%, respectively (**Table 1**). The ubiquinol/sum ratio was slightly lower after the ubiquinol supplementation, but the difference between 2 supplements did not reach statistical significance.

In PBMC, the supplementation did not lead to a significant change in ubiquinol, ubiquinone, sum, and ubiquinol/sum ratio, as well as ATP content (**Table 2**). Plasma MDA, a biomarker of lipid peroxidation and oxidative stress, tended to be lower after the supplementation (P = 0.1) from 0.82 to 0.78 µmol/L when all data were combined for the statistical analysis (**Fig. 2**). Plasma FRAP (from 869 to 849 Fe^{2+} µmol/L) and total thiol (from 260 to 261 µmol/L) were not altered.

Correlation tests showed that ubiquinol status in PBMC, but not plasma, was inversely associated with MDA, a biomarker of lipid peroxidation and oxidative stress. Plasma ubiquinol and ubiquinone were not correlated with plasma FRAP and total thiol (**Fig. 3**).

Discussion

Co-enzyme Q10 is an important endogenous molecule mainly due to its fundamental role in the electron transport chain for the ATP production. In addition, it acts as a potent lipophilic antioxidant to protect against radical-induced lipid, protein, and DNA oxidation, which in turn promotes the use of CoQ10 as a supplement to prevent and attenuate the pathology of cardiovascular and neurodegenerative diseases, improve exercise performance, and reduce exercise-induced muscular injury.[4,26-28] One of the major issues concerning the use of all dietary supplements for health prevention and promotion is bioavailability of active constituents

that can reach and accumulate in target organs. For example, higher than "normal" plasma CoQ10 concentration, e.g., >2.78 μmol/L, is required to promote CoQ10 uptake into peripheral tissues and to cross the blood-brain barrier.[7] The bioavailability of CoQ10 supplement is influenced by dosage, dietary fat, vitamin E intake, delivery vehicle, and chemical state (form).[29,30] In this study, we found that CoQ10 supplement in the ubiquinol form could achieve this threshold of 2.78 μmol/L, but not the ubiquinone, in the older adults who are likely to use this supplement.

CoQ10 mainly exists in the ubiquinol form in mitochondria and plasma. Thus, prior to the exertion of its bioactions, ubiquinone as the common CoQ10 form formulated in dietary supplements must be reduced to ubiquinol through a number of enzymes such as glutathione reductase, thioredoxin reductase, and NAD(P)H quinone oxidoreductase 1[1]. Since all these enzymes contribute to the antioxidant defence system, redox status may influence the bioavailability of CoQ10 and consequent bioefficacy in target tissues. Miles et al. reported that there was an age-related decrease in CoQ10 redox ratio after 18 years, probably related to oxidative stress associated with the development of hyperlipidemia and coronary heart disease.[31] Our study showed that 14-day supplementation of ubiquinol at 200 mg/day led to a significantly larger increase in total CoQ10 and ubiquinone concentrations in plasma of older men as compared to ubiquinone supplement (**Supplemental Fig 2**). These results appear to be consistent with the finding of Langsjoen et al. study with younger subjects aged 29-50 y, showing that supplemental ubiquinol at the dose of 200 mg/day was significantly better absorbed than ubiquinone.[32] Furthermore, the results of 2 acute pharmacokinetics studies illustrated that ubiquinol was more bioavailable than ubiquinone.[14,16] However, this study also showed that the superiority of ubiquinol supplement did not fare better than ubiquinone when 2 forms were delivered in the same formulation. Factors such as subject characteristics (old vs. young), dose (200 mg/d vs. 180 mg), and duration (2 weeks vs. acute) may influence the bioavailability of CoQ10.[13] As compared to Miles et al. study, repeatedly daily dosing, such as 2 weeks administered in our study, may be required to illustrate the merit of ubiquinol over ubiquinone in the bioavailability.[16]

In the era of personalized nutrition, it is well appreciated that bioavailability and consequent bioefficacy of nutrients differ widely among individuals due to the influence of an array of genetic, biochemical, and physiological factors and microbiota in the gut.[33] For example, age, race, and gender have been reported to influence CoQ10 status.[31,32,34] Total CoQ10 in plasma ranges from 0.40 to 1.91 μmol/L.[13] Before the intervention, plasma CoQ10 status of our study subjects fell in this range. At the end of 2-week supplementation, the CoQ10 supplements improved CoQ10 status in the study cohort but the magnitude of the change was varied widely among individuals. Such a wide variation is consistent with the high standard deviations reported in the literature, probably due to differences in the ability to absorb CoQ10 among people.[35,36] Interestingly, we noted the degree of the increase in plasma ubiquinone after ubiquinol supplementation was similar to that in plasma ubiquinol as compared to 1-fold difference after ubiquinone supplementation. It is plausible that this divergence in plasma ubiquinone increase after CoQ10 supplementations may be attributed to the capacity of CoQ10 recycling in older adults.

Plasma or serum is commonly used as a surrogate for the status of nutrients or molecules in tissues or whole body but the positive associations only exist in some but not all. In the case of CoQ10, lymphocytes, which constitute mitochondria and contain a significant amount of CoQ10, was also considered as a surrogate for tissue CoQ10 status as CoQ10 content in lymphocytes was increased by CoQ10 supplementation with concomitant protection against oxidative DNA damage.[13,37] In opposite to the supplementation-associated increase in plasma CoQ10, we did not find the supplementation elevated ubiquinol and ubiquinone in PBMC. These results appear conflicting with the previous suggestion that lymphocytes reflected CoQ10 status in tissues, particularly in the heart and brain where CoQ10 is in high demand.[13] Our result also did not agree with the finding of Niklowitz et al. study, in which CoQ10 supplementation increased CoQ10 status in white blood cells and platelets in women taking 3 mg/kg/d Sanomit® Q10 for 28 days.[38] CoQ10 levels have been found to decline gradually with advanced age.[6] Thus, the discrepancy in the PBMC results between younger women (mean 39 years old) in Niklowitz et al. study and older adults (63.9 years old) in ours may be attributed to age.

Oxidative stress is associated with aging and a plethora of chronic diseases, such as cardiovascular diseases, cancers, and cognitive decline. The status of oxidative stress can be assessed by using an array of biomarkers, including 8-oxo-deoxyguanosine, isoprostanes, protein carbonyl. Moreover, the ratio of reduced and oxidized glutathione and ubiquinol and total CoQ10 are considered an index of redox status. Rivara et al. reported that a high dose of CoQ10 supplementation (1200 mg/day) decreased plasma $F_{2\alpha}$-isoprostanes as compared to placebo in 65 patients undergoing weekly maintenance hemodialysis, illustrating the antioxidant protection of CoQ10.[39] The antioxidant effect of CoQ10 was also noted in strenuous exercise-induced oxidative stress when younger adults were supplemented with 200 mg/d ubiquinol for 2 weeks [28] and in patients with diabetic nephropathy who taking 100 mg/day CoQ10 for 12 weeks.[40] However, neither ubiquinol nor ubiquinone supplement modulated the measured oxidative stress biomarkers, including MDA, FRAP, and total thiol, in our study. It is plausible that these biomarkers may not so sensitive to detect changes in oxidative stress status of the study participants. Langsjoen et al. noted that supplemental ubiquinol increased the ratio of plasma ubiquinol to total CoQ10, indicative of the enhanced capacity of antioxidant defense.[32] Once again, such a change was not noted in our study, consistent with the oxidative stress biomarkers.

There were some limitations in this study. Due to the budget constraint, the current sample size was relatively modest so that a robust human trial is warranted to confirm our finding. CoQ10 values in plasma have been presented with and without the adjustment of plasma cholesterol. Whether the significance noted in the current data form would be different when the data were adjusted with cholesterol also warrants further research. While oxidative stress status was assessed using MDA in this study, other biomarkers such as 8-oxo-deoxyguanosine and isoprostanes shall be considered because of their considerably better validity in the measurement of oxidative stress status.

Conclusions

The bioefficacy of the CoQ10 supplement has been under scrutiny because of its low absorption and bioavailability.[7] Pharmaceutical technologies, such as solubilized formulations, have been developed to improve the bioavailability of ubiquinone, which is the common CoQ10 supplemental form.[41] Since it is more water soluble, ubiquinol, the reduced form of ubiquinone has been demonstrated to be more bioavailable in acute pharmacokinetic studies.[14,32] Our short-term supplementation study confirms that ubiquinol is superior to ubiquinone to increase the status of total CoQ10 in adults older than 55 y. However, neither ubiquinone nor ubiquinol affects CoQ10 status in PBMC and oxidative stress biomarkers in plasma.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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Captions

Figure 1. The change in plasma ubiquinol status of individual subjects after the supplementation. *P-values for the difference of the "After" values between ubiquinol and ubiquinone supplement, tested using the MIXED model with treatment, sequence, and period as independent variables.

Figure 2. Neither ubiquinol nor ubiquinone supplement affected plasma MDA.

Figure 3. The correlation of ubiquinol and ubiquinone with FRAP and total thiol in plasma and PBMC (prq: ubiquinol in plasma; pxq:ubiquinone in plasma; ptot: total coq10 in plasma; proqto: ratio of ubiquinol to total coq10 in plasma; crq: ubiquinol in PBMC; cxq:ubiquinone in PBMC; ctot: total coq10 in PBMC; croqto: ratio of ubiquinol to total coq10 in PBMC; atp: ATP in PBMC; atpc: ATP in PBMC treated with CCCP).

Figure 1.

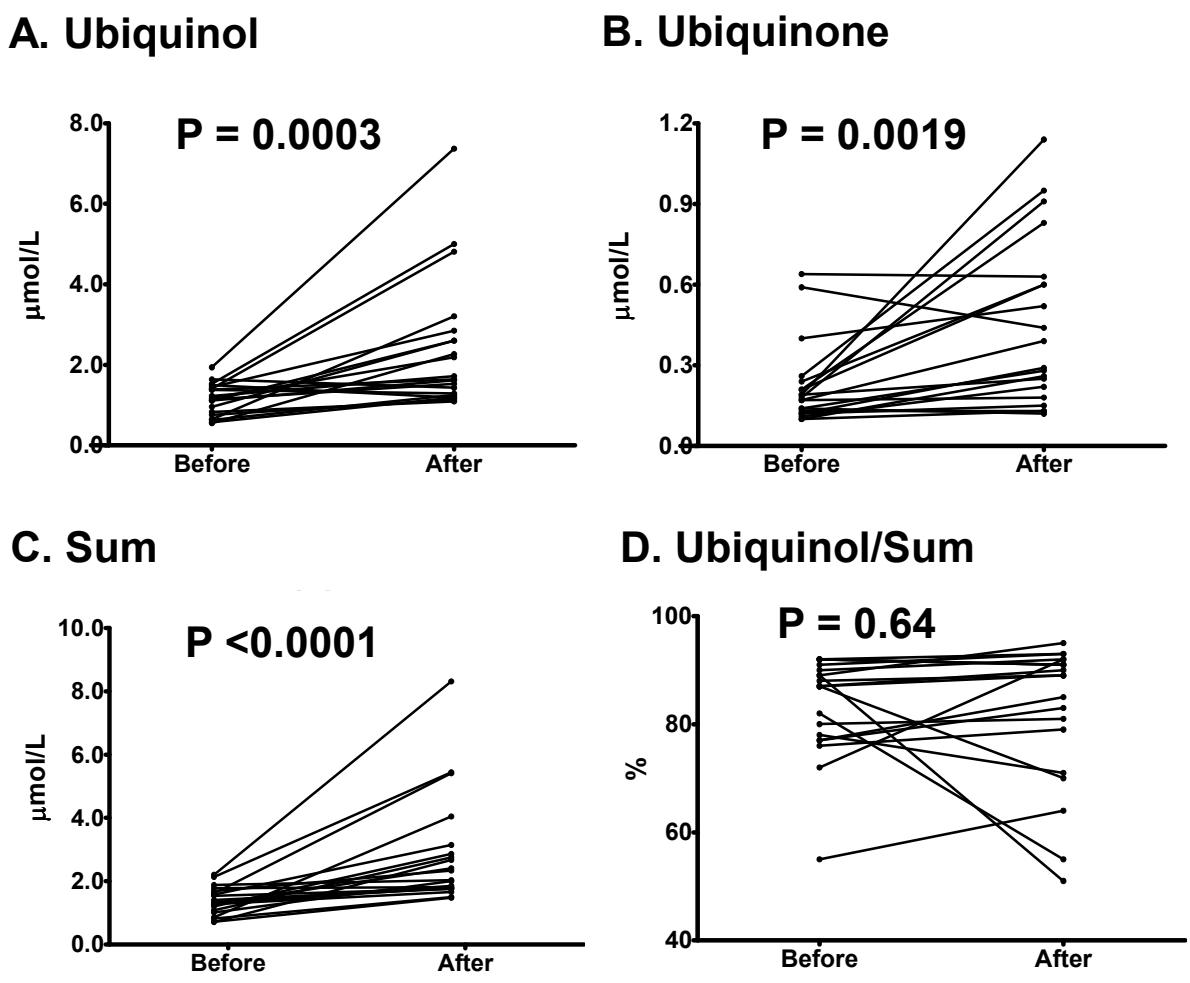
A. Ubiquinol
P = 0.0003
µmol/L
8.0
6.0
4.0
2.0
0.0
Before
After
B. Ubiquinone
P = 0.0019
µmol/L
1.2
0.9
0.6
0.3
0.0
Before
After
C. Sum
P <0.0001
µmol/L
10.0
8.0
6.0
4.0
2.0
0.0
Before
After
D. Ubiquinol/Sum
P = 0.64
%
100
80
60
40
Before
After

Figure 2.

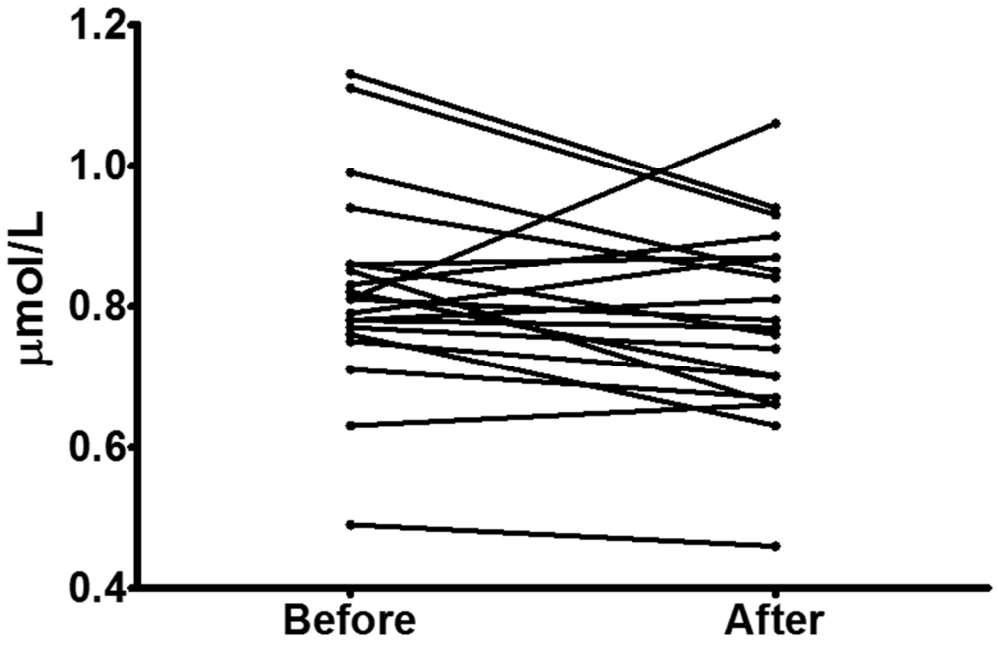

Figure 3.

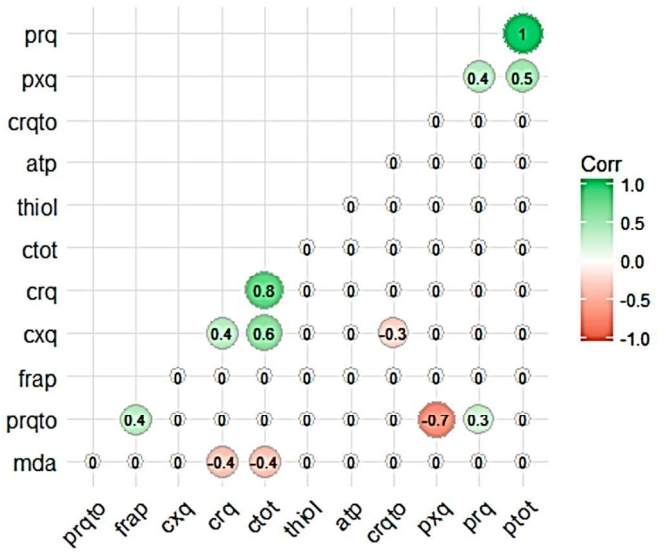
prq
pxq
crqto
atp
thiol
ctot
crq
cxq
frap
prqto
mda
prqto
frap
cxq
crq
ctot
thiol
atp
crqto
pxq
prq
ptot
Corr
1.0
0.5
0.0
-0.5
-1.0

Table 1. Plasma ubiquinol and ubiquinone status in older men taking 200 mg/day ubiquinol or ubiquinone for 2 weeks[1]

	Ubiquinol		Ubiquinone		P-value*
	Before	After	Before	After	
Ubiquinol (μmol/L)	1.12 ± 0.44	2.80 ± 2.00	1.18 ± 0.35	1.99 ± 1.11	0.085
Ubiquinone (μmol/L)	0.22 ± 0.16	0.60 ± 0.35	0.22 ± 0.16	0.30 ± 0.18	0.012
Sum (μmol/L)	1.34 ± 0.45	3.41 ± 2.08	1.40 ± 0.45	2.29 ± 1.16	0.027
Ubiquinol/Sum (%)	83.0 ± 11.1	78.5 ± 16.1	84.3 ± 7.5	86.0 ± 8.8	0.135

[1]Data are expressed as mean ± SD (N = 10).

*P-values for the difference of the "After" values between ubiquinol and ubiquinone supplement, tested using the MIXED model with treatment, sequence, and period as independent variables.

Table 2. Ubiquinol and ubiquinone status in peripheral blood mononuclear cells (PBMC) of older men taking 200 mg/day ubiquinol or ubiquinone for 2 weeks[1]

	Ubiquinol		Ubiquinone		P-value*
	Before	After	Before	After	
Ubiquinol ($pmol/10^6$ cells)	6.10 ± 2.53	6.63 ± 2.19	6.08 ± 2.77	6.46 ± 2.54	0.347
Ubiquinone ($pmol/10^6$ cells)	3.17 ± 1.09	3.61 ± 1.65	3.18 ± 1.51	3.57 ± 1.60	0.094
Sum ($pmol/10^6$ cells)	9.27 ± 3.42	10.24 ± 3.27	9.26 ± 3.98	10.03 ± 3.45	1.000
Ubiquinol/Sum (%)	64.8 ± 8.1	64.9 ± 11.3	65.2 ± 8.3	63.8 ± 12.0	0.648

[1]Data are expressed as mean ± SD (N = 10).

*P-values for the difference of the "After" values between ubiquinol and ubiquinone supplement, tested using the MIXED model with treatment, sequence, and period as independent variables.

Ubiquinol is a better form than ubiquinone to maintain CoQ10 status in older adults.