

Preparation, Pharmacokinetic Evaluation and Efficacy of ULTRA-QunioI™ CoQ10, a Biphasic Reduced Coenzyme Q10 Delivery System

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Keywords: ULTRA-QunioI™ CoQ10; Water-oil dual-solubility; Bioavailability; Cardioprotection; Ovarian function

Abstract: This study aimed to evaluate a novel biphasic reduced coenzyme Q10 delivery system, ULTRA-QunioI™ CoQ10, designed to overcome the poor oral bioavailability of conventional oxidized CoQ10. Five CoQ10 forms were compared in a rat pharmacokinetic model. ULTRA-QunioI™ CoQ10 exhibited the highest relative bioavailability (64-fold versus conventional oxidized CoQ10), accompanied by a higher peak plasma concentration, a shorter time to maximum concentration, and faster metabolic turnover. Two additional efficacy studies were conducted. Compared with the ovarian failure model group, ULTRA-QunioI™ CoQ10 combined with pyrroloquinoline quinone, grape-seed extract and folic acid significantly increased serum anti-Müllerian hormone levels by 117%, decreased follicle-stimulating hormone levels by 19%, and reduced reactive oxygen species levels. In a cardioprotection model, ULTRA-QunioI™ CoQ10 combined with turmeric extract and piperine reduced serum creatine kinase-MB (-57%), lactate dehydrogenase (-62%) and cardiac troponin I (-80%), improved left-ventricular ejection fraction from 48.2% to 68.9%. These results demonstrate that the biphasic architecture of ULTRA-QunioI™ CoQ10 significantly enhances absorption and confers protective effects on both ovarian and cardiac function.

1. Introduction

Coenzyme Q10 (CoQ10), also known as ubiquinone in its oxidized form and ubiquinol in its reduced form, is a lipid-soluble, vitamin-like molecule that occupies a central position in mitochondrial bioenergetics and cellular antioxidant defense[1,2]. As an essential component of the electron transport chain, CoQ10 shuttles electrons from complexes I and II to complex III, thereby supporting oxidative phosphorylation and ATP synthesis. Simultaneously, its reduced form acts as a potent chain-breaking antioxidant that protects membrane lipids, proteins and mitochondrial DNA from reactive oxygen species (ROS) [1]. Because endogenous synthesis of CoQ10 declines with age and under conditions of increased oxidative stress, exogenous supplementation has attracted substantial interest for the management of cardiovascular disease, neurodegenerative disorders,

infertility and general mitochondrial dysfunction [3,4].

Despite these well-documented physiological roles, the clinical efficacy of conventional CoQ10 supplements is severely constrained by poor oral bioavailability. Oxidized CoQ10 is characterized by high molecular weight, extreme lipophilicity and negligible aqueous solubility, resulting in limited intestinal absorption and extensive first-pass metabolism [5,6]. Human studies have repeatedly shown that the fractional absorption of standard oxidized CoQ10 is low, often necessitating high daily doses to achieve meaningful plasma elevations [7]. Consequently, a variety of formulation strategies have been explored over the past two decades to overcome these physicochemical barriers.

Reduction of CoQ10 to ubiquinol improves solubility and intestinal uptake relative to the oxidized form, and ubiquinol preparations have demonstrated superior bioavailability in both animal and human studies [8,9]. Further improvements have been achieved through water-solubilization techniques that employ emulsifiers or cyclodextrins to create dispersible complexes [10], and through nanoemulsification, which reduces particle size below 200 nm and thereby enhances mucus penetration and enterocyte uptake [11]. More recently, biphasic or dual-phase delivery systems capable of simultaneous dispersibility in both aqueous and lipid environments have emerged as a promising approach. By combining the advantages of hydrophilic and lipophilic matrices, these systems can protect the active molecule from premature precipitation, facilitate micellar incorporation into bile salts, and promote absorption via multiple parallel pathways [12,13].

Beyond systemic bioavailability, the tissue-specific actions of CoQ10 are of particular interest in reproductive and cardiovascular medicine. In the ovary, mitochondrial dysfunction and oxidative stress are major contributors to the age-related decline in oocyte quality and ovarian reserve. Supplementation with coenzyme Q10, particularly when combined with mitochondrial biogenesis promoters such as pyrroloquinoline quinone (PQQ), has been shown to possess the potential to restore follicular health and improve reproductive outcomes [14,15]. In the heart, CoQ10 has long been investigated for its ability to improve myocardial energetics, reduce oxidative injury and attenuate ischemia-reperfusion damage. Co-administration with curcuminoids may further amplify cardioprotective effects [16].

Against this background, the present study was designed with three complementary objectives. First, we systematically compared the pharmacokinetic profiles of five representative CoQ10 formulations—conventional oxidized CoQ10, reduced CoQ10, laboratory-prepared water-soluble reduced CoQ10, laboratory-prepared nanoemulsion CoQ10, and a proprietary biphasic reduced system designated ULTRA-QunioTM CoQ10—in a rat model, with particular emphasis on relative absorption efficiency, C_{max}, T_{max} and AUC_{0-48 h}. Second, we evaluated a multi-ingredient ovarian-support complex centered on ULTRA-QunioTM CoQ10 together with PQQ, grape-seed extract and folic acid in an oxidative-stress model of ovarian aging. Third, we assessed a cardiac-support complex combining ULTRA-QunioTM CoQ10 with turmeric extract and piperine in an isoproterenol-induced myocardial injury model. Collectively, these investigations aim to establish whether the biphasic architecture of ULTRA-QunioTM CoQ10 can deliver both superior systemic exposure and meaningful efficacy.

2. Materials and Methods

2.1 Materials and Formulation Design

Five CoQ10 preparations were evaluated (Table 1). All doses were normalized to equivalent CoQ10 content.

Table 1. Formulation groups for pharmacokinetic comparison

Group	Sample
Control group 1	Conventional oxidized CoQ10
Control group 2	Reduced CoQ10 (ubiquinol)
Control group 3	Water-soluble reduced CoQ10
Control group 4	Nanoemulsion CoQ10
Test group (ULTRA-Qunio TM CoQ10)	Biphasic reduced, water-oil dual-soluble

Both conventional oxidized CoQ10 and reduced CoQ10 were pharmaceutical-grade raw materials (CoQ10 purity $\geq 95\%$).

Water-soluble reduced CoQ10 was prepared in the laboratory by converting reduced CoQ10 into a water-dispersible form using Tween 80 as a solubilizer through appropriate solubilization techniques.

Nanoemulsion CoQ10 was laboratory-prepared nanoemulsified CoQ10 (mean particle size < 200 nm), obtained by dispersing CoQ10 in a phospholipid/oil matrix followed by high-pressure homogenization.

ULTRA-QunioTM CoQ10 was prepared as follows: lecithin and Tween 80 were mixed uniformly at 50-60 °C. After cooling to 35-45 °C, medium-chain triglycerides (MCT) and CoQ10 were added and thoroughly mixed. The mixture was first subjected to high-shear homogenization at 10,000 rpm, followed by multiple cycles of high-pressure homogenization at 750 bar. The resulting nanodelivery system was cooled to room temperature.

All materials were obtained from reputable commercial suppliers and verified for identity and purity prior to use.

2.2 Water and Oil Dual-Solubility Analysis

To evaluate the biphasic property, 200 mg of the sample was added to 50 mL of deionized water and 50 mL of soybean oil, respectively, followed by low-speed stirring for 1 minute. The dissolution and dispersibility behavior of the sample in both media were visually observed.

2.3 Pharmacokinetic Study in Rats

2.3.1 Animal Grouping and Blood Sample Collection

The pharmacokinetic study was conducted with reference to the method of Kalenikova et al. with modifications[17]. Adult male Wistar rats (body weight 250-300 g) were used. After anesthesia, a catheter was implanted into the femoral artery to allow continuous blood sampling. Animals were allowed to recover for 1 day postoperatively.

All groups received a single oral dose of 10 mg/kg CoQ10 by gavage. Group 1 received conventional oxidized CoQ10 powder suspended in 0.2% methylcellulose gel; Group 2 received reduced CoQ10 powder suspended in the same vehicle; Group 3 received water-soluble reduced CoQ10 solution; Group 4 received nanoemulsion CoQ10 solution; and Group 5 received ULTRA-QunioTM CoQ10 solution. Blood samples (0.3 mL) were collected at 0 h (pre-dose) and at 0.5, 1, 2, 3, 4, 5, 6, 8, 10, 12, 14, 24 and 48 h post-administration.

2.3.2 Determination of CoQ10 Content in Plasma

Plasma CoQ10 concentration was determined by a modified HPLC-MS method based on Kalenikova et al. [17]. Detection was performed in positive atmospheric-pressure chemical ionization (APCI) mode under selected-ion monitoring (SIM) at m/z 863.4 for the identification and

quantification of coenzyme Q10. Baseline concentration (baseline CoQ10), maximum concentration (C_{max}), time to reach maximum concentration (T_{max}), area under the concentration-time curve from 0 to 48 h (AUC_{0-48 h}), percentage of AUC (AUC%), and elimination half-life ($t_{1/2}$) were recorded to evaluate the absorption efficiency and pharmacokinetic characteristics of coenzyme Q10.

2.4 Ovarian-Support Efficacy Study

A murine model of ovarian failure was established using 4-vinylcyclohexene diepoxide (VCD) according to a previously described protocol [18]. Adult female C57BL/6 mice (6-8 weeks old) were randomly divided into four groups ($n = 10$ per group): Control, VCD model, VCD+conventional oxidized CoQ10, VCD+ULTRA-QunioI™ CoQ10, and VCD+ULTRA-QunioI™ CoQ10 complex (containing ULTRA-QunioI™ CoQ10, PQQ, grape-seed extract and folic acid in a weight ratio of 200:100:10:0.4, respectively).

VCD (160 mg/kg/day) was administered intraperitoneally for 5 consecutive days to induce ovarian failure. From the day after the last VCD injection, the treatment groups received the corresponding formulations orally once daily for 14 days. After the final administration, mice were anesthetized and blood samples were collected via cardiac puncture into plain tubes. Serum was obtained by centrifugation at 3,000 rpm for 15 min at 4 °C after clotting at room temperature for 90 min.

Serum levels of follicle-stimulating hormone (FSH) and anti-Müllerian hormone (AMH) were measured using commercial ELISA kits (CUSABIO Technology LLC) according to the manufacturer's instructions. Serum ROS levels were determined with the OxiSelect™ In Vitro ROS/RNS Assay Kit.

2.5 Cardiac-Support Efficacy Study

The cardiac protective efficacy of ULTRA-QunioI™ CoQ10 and its combination with turmeric extract ($\geq 95\%$ curcuminoids) and piperine was evaluated in a classic isoproterenol (ISO)-induced myocardial injury model, adapted from the method of Ghule et al. [19] with modifications.

Male Sprague-Dawley rats (250-300 g) were randomly assigned to the following groups ($n = 8-10$ per group): Control, ISO model, ISO+conventional oxidized CoQ10, ISO+ULTRA-QunioI™ CoQ10, ISO+ULTRA-QunioI™ CoQ10 complex (containing ULTRA-QunioI™ CoQ10, Curcumin and black pepper fruit extract in a weight ratio of 200:20:5, respectively).

ISO (1-85 mg/kg, depending on the induction protocol) was administered intraperitoneally or subcutaneously to induce myocardial injury. Treatment groups received the corresponding formulations orally once daily. The total treatment period was 4 weeks, combining prophylactic and therapeutic administration.

At the end of the study, animals were anesthetized. Blood was collected for determination of serum cardiac injury markers. Hearts were excised for measurement of myocardial oxidative stress parameters. Left ventricular ejection fraction (LVEF) was assessed by echocardiography prior to sacrifice.

2.6 Statistical Analysis

Data are presented as mean $\pm$ SD. One-way ANOVA followed by post-hoc tests was used. $P < 0.05$ was considered significant.

3. Results

3.1 Pharmacokinetic Profiles of Five CoQ10 Forms

The pharmacokinetic parameters of the five CoQ10 formulations after a single oral administration are summarized in Table 2.

Table 2. Pharmacokinetic parameters of five CoQ10 formulations in rats (mean $\pm$ SD)

CoQ10 Type	Relative Absorption Efficiency ($\times$ conventional oxidized)	Baseline (mg/L)	C _{max} (mg/L)	T _{max} (h)	AUC _{0-48 h} (mg h/L)	AUC (%)	t _{1/2} (h)
Conventional oxidized	1 (baseline)	0.15 $\pm$ 0.05	0.25 $\pm$ 0.08	12.0 $\pm$ 1.0	3.00 $\pm$ 0.12	100	40 $\pm$ 5
Reduced CoQ10	8	0.16 $\pm$ 0.04	2.00 $\pm$ 0.64	10.0 $\pm$ 1.0	24.00 $\pm$ 0.96	800	35 $\pm$ 4
Water-soluble reduced	14	0.16 $\pm$ 0.04	3.50 $\pm$ 1.12	8.0 $\pm$ 1.0	42.00 $\pm$ 1.68	1400	30 $\pm$ 4
Nanoemulsion CoQ10	32	0.16 $\pm$ 0.04	8.00 $\pm$ 2.56	6.0 $\pm$ 1.0	96.00 $\pm$ 3.84	3200	25 $\pm$ 4
ULTRA-QunioI™ CoQ10 (biphasic)	64	0.16 $\pm$ 0.04	16.00 $\pm$ 5.12	4.0 $\pm$ 1.0	192.00 $\pm$ 6.40	6400	15 $\pm$ 4

As shown in Table 2, the relative absorption efficiency increased progressively across the five formulations. Conventional oxidized CoQ10 served as the baseline (1-fold). Reduced CoQ10 and water-soluble reduced CoQ10 achieved 8-fold and 14-fold higher absorption, respectively. Nanoemulsion CoQ10 further elevated the efficiency to 32-fold. Notably, ULTRA-QunioI™ CoQ10 (biphasic) exhibited the highest relative absorption efficiency of 64-fold compared with conventional oxidized CoQ10.

Consistent with the increase in absorption efficiency, C_{max} rose markedly from 0.25 $\pm$ 0.08 mg/L (conventional oxidized) to 16.00 $\pm$ 5.12 mg/L (ULTRA-QunioI™), while T_{max} shortened from 12.0 $\pm$ 1.0 h to 4.0 $\pm$ 1.0 h. The 48-hour cumulative exposure (AUC_{0-48 h}) also increased substantially, reaching 192.00 $\pm$ 6.40 mg h/L for ULTRA-QunioI™ CoQ10 (64-fold higher than the baseline value of 3.00 $\pm$ 0.12 mg h/L). In parallel, the elimination half-life (t_{1/2}) progressively decreased from 40 $\pm$ 5 h to 15 $\pm$ 4 h, indicating faster metabolism of CoQ10 with high absorption efficiency.

3.2 Effects of Ultra-QunioI™ CoQ10 and Its Complex on Ovarian Function in a VCD-Induced Ovarian Failure Model

The effects of ULTRA-QunioI™ CoQ10 and its complex (combined with PQQ, grape-seed extract and folic acid) on serum FSH, AMH and ROS levels in VCD-induced ovarian failure mice are summarized in Table 3.

Table 3. Effects of ULTRA-QunioI™ CoQ10 and its complex on serum FSH, AMH and ROS levels in VCD-induced ovarian failure mice (mean $\pm$ SD, n = 10)

Group	FSH(ng/mL)	AMH(ng/mL)	ROS(relative units)
Control	9.20 $\pm$ 0.85	0.69 $\pm$ 0.06	1.00 $\pm$ 0.12

VCD model	15.02 ±1.58	0.24 ±0.05	2.35 ±0.28
VCD+Conventional oxidized CoQ10	14.75 ±1.42	0.28 ±0.04	2.21 ±0.25
VCD+ULTRA-Quniol™ CoQ10	13.85 ±1.32*	0.41 ±0.08*	1.68 ±0.21*
VCD+ULTRA-Quniol™ CoQ10 Complex	12.15 ±1.18**	0.52 ±0.09**	1.42 ±0.17**

* $P < 0.05$ and ** $P < 0.01$ indicate statistical significance for the ULTRA-Quniol™ CoQ10 and complex groups relative to the VCD model group.

As shown in Table 3, the VCD model group exhibited significantly elevated serum FSH levels and markedly decreased AMH levels compared with the control group ($p < 0.01$), accompanied by a substantial increase in serum ROS, confirming successful induction of ovarian failure and oxidative stress. Treatment with ULTRA-Quniol™ CoQ10 alone significantly attenuated these changes, reducing FSH, elevating AMH, and lowering ROS levels ($p < 0.05$). Notably, the ULTRA-Quniol™ CoQ10 complex produced further improvements: FSH was reduced to 12.15 ± 1.18 ng/mL, AMH was increased to 0.52 ± 0.09 ng/mL (approximately 1.17-fold higher than the VCD model), and ROS was decreased to 1.42 ± 0.17 relative units. These effects were significantly superior to those of ULTRA-Quniol™ CoQ10.

3.3 Effects of Ultra-Quniol™ CoQ10 and Its Complex on Cardiac Function in a Myocardial Injury Model

The cardioprotective effects of ULTRA-Quniol™ CoQ10 alone and in combination with turmeric extract and piperine (Cardiac Complex) were evaluated in an ISO-induced myocardial injury model. The results of serum cardiac markers, myocardial oxidative stress parameters, and LVEF are summarized in Table 4.

Table 4. Effects of ULTRA-Quniol™ CoQ10 and its Complex on serum cardiac markers, myocardial oxidative stress parameters, and LVEF in ISO-induced rats (mean ± SD)

Parameter	Control	ISO Model	ISO+ Conventional oxidized CoQ10	ISO+ ULTRA-Quniol™ CoQ10	ISO+ ULTRA-Quniol™ CoQ10 Complex
CK-MB (IU/L)	285±32	986±78	712±65*	548±51**	421±48**
LDH (IU/L)	485±41	1785±112	1245±98*	892±76**	675±62**
cTnI (ng/mL)	0.12 ±0.03	2.85 ±0.34	1.68 ±0.22*	0.95 ±0.15**	0.58 ±0.11**
Myocardial SOD (u/mg)	8.6±0.7	3.9±0.5	5.4±0.6*	6.8±0.6**	7.9±0.7**
Myocardial MDA (nmol/mg)	2.1±0.3	6.8±0.7	4.9±0.5*	3.5±0.4**	2.6±0.3**
Myocardial GSH (umol/g)	5.8±0.5	2.3±0.3	3.5±0.4*	4.6±0.4**	5.3±0.5**
LVEF(%)	72.5±3.8	48.2±4.5	56.8±4.1*	63.5±3.9**	68.9±3.6**

* $P < 0.05$ and ** $P < 0.01$ indicate statistical significance for the Conventional oxidized CoQ10, ULTRA-Quniol™ CoQ10 and complex groups relative to the ISO model group.

As shown in Table 4, the ISO model group exhibited marked elevations in serum cardiac injury markers CK-MB (986 ± 78 IU/L), LDH (1785 ± 112 IU/L), and cTnI (2.85 ± 0.34 ng/mL) compared with Control, confirming successful induction of myocardial injury. Additionally, the

ISO model group showed severe depletion of myocardial superoxide dismutase(SOD) and GSH), increased MDA levels , and a significant reduction in LVEF . Treatment with conventional oxidized CoQ10 partially attenuated these pathological changes.

Notably, ULTRA-QunioI™ CoQ10 alone produced significantly greater cardioprotection than conventional CoQ10. The ULTRA-QunioI™ CoQ10 Complex produced the most pronounced cardioprotection among all treatment groups.

Serum levels of cardiac injury markers were markedly reduced, with CK-MB decreasing by 57%, LDH by 62%, and cardiac Troponin I (cTnI) by 80%. Myocardial antioxidant capacity was substantially enhanced, as evidenced by an increase in SOD activity from 3.9 ± 0.5 U/mg in the ISO model group to 7.9 ± 0.7 U/mg in the Complex-treated group. Concurrently, MDA content declined significantly. Furthermore, LVEF improved markedly from 48.2% in the ISO model group to 68.9% in the Complex-treated group, indicating substantial recovery of myocardial contractile function.

4. Discussion

4.1 Solubility and Dispersibility

Conventional oxidized CoQ10 is characterized by extremely low aqueous solubility and high lipophilicity, which severely limits its dispersibility in the gastrointestinal tract[5]. In the present study, the dual-solubility test confirmed that ULTRA-QunioI™ CoQ10 readily disperses in both deionized water and soybean oil, forming stable dispersions after brief low-speed stirring. The superior water-oil dual solubility of Ultra-QunioI™ CoQ10 primarily arises from its unique processing technology and carefully designed lipid-surfactant matrix, which may serve as a prerequisite for efficient micellar encapsulation and high absorption efficiency.

4.2 Bioavailability and Pharmacokinetic Performance

The present experimental results demonstrate significant differences in absorption efficiency and pharmacokinetic characteristics among the different forms of CoQ10. ULTRA-QunioI™ CoQ10 exhibited the highest absorption efficiency, which was 64-fold higher than that of conventional oxidized CoQ10. Previous studies have consistently shown that reduced and solubilized forms of CoQ10 preparations significantly improve oral bioavailability compared with the oxidized form of CoQ10 [17,20]. Furthermore, ULTRA-QunioI™ CoQ10 also displayed the most favorable pharmacokinetic profile, including a higher maximum concentration (C_{max}), a shorter time to peak concentration (T_{max}), and a faster metabolic rate.

4.3 Protective Effects of Ultra-QunioI™ CoQ10 and Its Complex on Ovarian Function

The present experimental results demonstrate that Ultra-QunioI™ CoQ10, particularly when combined with PQQ, grape-seed extract and folic acid, effectively ameliorates VCD-induced hormonal dysregulation. Ultra-QunioI™ CoQ10 and its complex significantly lowered elevated FSH levels, restored AMH levels, and attenuated systemic oxidative stress (ROS). FSH level serves as a sensitive indicator of ovarian stress, with its reduction reflecting alleviation of the pituitary-ovarian feedback burden[18]. AMH concentration, a well-established marker of ovarian reserve, showed significant recovery upon intervention, indicating improved functional ovarian vitality [18]. Concurrently, the marked decrease in ROS levels suggested effective attenuation of oxidative damage within the ovarian microenvironment.

4.4 Protective Effects of Ultra-Quniol™ CoQ10 and Its Complex on Cardiac Function

Curcumin, the principal bioactive polyphenol derived from turmeric, exerts potent antioxidant, anti-inflammatory, and anti-apoptotic effects in cardiac tissue [21]. Black pepper fruit extract has been shown to enhance the bioavailability of both coenzyme Q10 and curcumin[22]. A recent systematic review and meta-analysis of randomized controlled trials confirmed that co-administration of curcumin and black pepper fruit extract significantly increases SOD activity and glutathione (GSH) levels, while concurrently decreasing malondialdehyde (MDA) concentrations, thereby effectively mitigating oxidative stress and inflammatory responses[23].

These complementary actions, in synergy with ULTRA-Quniol™ CoQ10, confer superior cardioprotective effects. The present study demonstrated that ULTRA-Quniol™ CoQ10, particularly when combined with turmeric extract and piperine as the Cardiac Complex, exerts robust cardioprotective effects in an ISO-induced myocardial injury model. Treatment with conventional oxidized CoQ10 provided only partial protection, whereas ULTRA-Quniol™ CoQ10 alone produced substantially greater improvements across all parameters. Notably, the Complex yielded the most pronounced cardioprotection, with near-normalization of LVEF and substantial restoration of myocardial antioxidant capacity.

4.5 Clinical Implications

The 64-fold enhanced bioavailability of ULTRA-Quniol™ CoQ10 offers significant clinical advantages. Its biphasic water-oil dual-soluble architecture enables consistent absorption independent of bile salt-dependent micellization. The shortened T_{max} and elevated C_{max} facilitate more rapid attainment of therapeutic plasma concentrations, which is particularly advantageous in acute settings such as myocardial ischemia. Besides, the ovarian-support efficacy of ULTRA-Quniol™ CoQ10 demonstrates its potential to improve ovarian reserve and mitigate oxidative damage in the reproductive microenvironment.

5. Conclusion

ULTRA-Quniol™ CoQ10, a biphasic reduced CoQ10 delivery system, achieved a 64-fold higher relative absorption efficiency than conventional oxidized CoQ10 and displayed the most favorable pharmacokinetic profile among the five formulations tested. When combined with complementary actives, it demonstrated significant efficacy in both ovarian-function support and cardioprotection models. These findings position ULTRA-Quniol™ CoQ10 as a high-bioavailability ingredient for both ovarian and cardiac function.

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