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A Ratio-Defined NVTIA CoQ10–BioPerine®–Vitamin E System for Improved Oral Delivery and Myocardial Redox Support

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ABSTRACT

Background: Cardiovascular disease remains the leading cause of death worldwide, and mitochondrial redox imbalance is an important component of myocardial dysfunction. Coenzyme Q10 (CoQ10) is mechanistically relevant to cardiac bioenergetics and antioxidant defense, but its clinical translation is constrained by poor oral bioavailability. Objective: We evaluated a ratio-defined NVTIA ternary system composed of CoQ10, BioPerine® (standardized piperine), and vitamin E, while placing its preclinical performance in the context of published formulation, pharmacokinetic, and cardiovascular outcome data. Methods: We examined three dosage-form embodiments disclosed for the ternary system and compared them with a binary CoQ10–piperine reference. We then summarized peer-reviewed studies on CoQ10 absorption, piperine-mediated exposure enhancement, formulation engineering, and heart-failure outcomes to assess translational plausibility. Results: In the available rat dataset, the ternary system increased relative plasma total CoQ10 to 1.19–1.38-fold and myocardial reduced CoQ10 to 1.79–2.13-fold versus the binary comparator. The 100:15:1 soft-capsule embodiment showed the highest myocardial enrichment. Published human data indicate that piperine coadministration can increase CoQ10 plasma exposure by about 30% after 21 days, and recent formulation studies confirm that lipid-based encapsulation materially improves CoQ10 bioaccessibility and cellular uptake. Meta-analytic and randomized clinical evidence further supports the clinical relevance of CoQ10 in chronic heart failure. Conclusion: The NVTIA ternary system is supported by a coherent mechanistic framework in which formulation engineering, piperine-assisted absorption, and vitamin E–linked redox support may jointly improve delivery of reduced CoQ10 to cardiac tissue. The preclinical signal is strong enough to justify prospective human validation, but the exact ternary ratio still requires registered clinical testing.

KEYWORDS

CoQ10; Piperine; Vitamin E; BioPerine®; Oral bioavailability; Myocardium; Ubiquinol; Heart failure

1. INTRODUCTION

Cardiovascular diseases are the leading cause of death globally and are estimated to account for 17.9 million deaths each year. This scale alone makes incremental gains in formulation performance clinically relevant when the target pathway is biologically plausible and the intervention is safe enough for long-term adjunctive use [1].

CoQ10 is indispensable to mitochondrial electron transport and also serves as a major lipid-soluble antioxidant. Its reduced form, ubiquinol, can help regenerate other antioxidants, including vitamins C and E, and high-energy organs such as the heart contain particularly high CoQ10 concentrations [2, 9]. In chronic heart failure, the rationale for CoQ10 supplementation is therefore both energetic and redox-related.

The main translational obstacle is oral delivery. CoQ10 is highly lipophilic, water-insoluble, and sensitive to formulation quality. Review-level evidence indicates that inadequate crystal dispersion can reduce bioavailability by about 75%, whereas solubilized, lipid-based, and self-emulsifying approaches can materially improve exposure [2, 3].

The NVTIA ternary system was conceived around this delivery problem. By pairing CoQ10 with standardized piperine and vitamin E in a ratio-defined platform, the formulation attempts to address three consecutive stages of the delivery pathway: intestinal absorption, systemic availability, and downstream maintenance of reduced CoQ10 in target tissue. In the present manuscript, we assess the available preclinical data for this platform and place those findings alongside peer-reviewed human and translational evidence.

2. MATERIALS AND METHODS

We evaluated three disclosed embodiments of the NVTIA ternary system spanning the active ratio range CoQ10: vitamin E:piperine = 100:12–18:1, together with a binary comparator lacking vitamin E. The formulations comprised a soft capsule in a medium-chain triglyceride carrier, a self-microemulsifying delivery system, and an orally disintegrating micro-tablet.

We retained the available preclinical endpoints exactly as reported for the platform: relative plasma total CoQ10 and relative myocardial reduced CoQ10 measured four hours after the final dose in a 7-day Sprague–Dawley rat study. These values are presented as fold-change versus the binary comparator.

For translational comparison, we extracted published data on four topics directly relevant to the ternary design: (i) CoQ10 oral bioavailability constraints and formulation strategies; (ii) piperine-mediated enhancement of CoQ10 exposure; (iii) the antioxidant interaction between CoQ10 and vitamin E; and (iv) randomized or meta-analytic cardiovascular outcome evidence.

3. RESULTS

3.1. Formulation Embodiments

Table 1. Formulation embodiments and key manufacturing features.

Group	Active ratio (CoQ10: VitE: Piperine)	Dosage form	Key manufacturing feature	Note
Embodiment 1	100:15:1	Soft capsule	Dissolution in MCT at 40–45°C; encapsulation	Highest myocardial enrichment
Embodiment 2	100:12:1	SMEDDS	Mixed oils + non-ionic surfactant	Nanoemulsion-style dispersion
Embodiment 3	100:18:1	OD micro-tablet	Ethanol dissolution; adsorption to silica; compression	Solidified lipophilic actives
Comparative	100:–:1	Soft capsule	Same route without vitamin E	Binary reference

3.2. Relative Systemic Exposure And Myocardial Accumulation

Table 2. Relative plasma total CoQ10 and myocardial reduced CoQ10.

Group	Relative plasma total CoQ10	Relative myocardial reduced CoQ10
Embodiment 1	1.26×	2.13×
Embodiment 2	1.38×	1.87×
Embodiment 3	1.19×	1.79×
Comparative	1.00×	1.00×

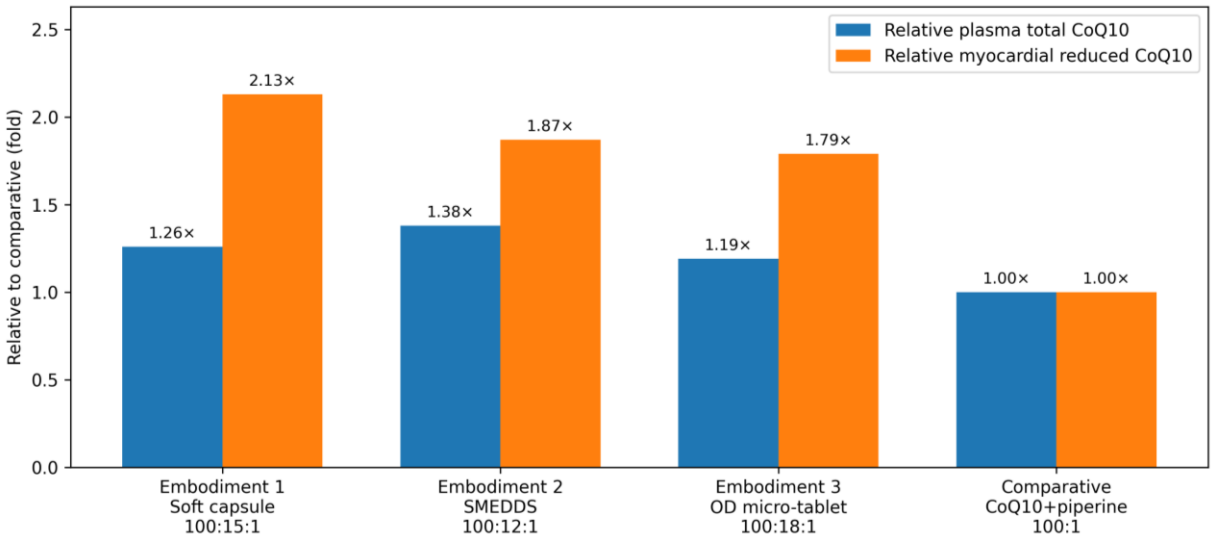

Figure 1. Relative exposure and myocardial accumulation in the available rat dataset

3.3. Mechanistic Framework

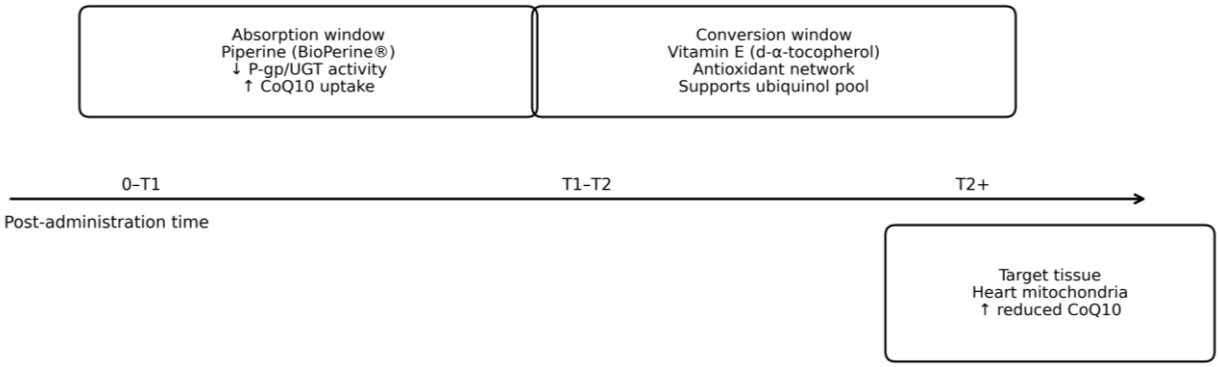

Figure 2. Conceptual temporal relay mechanism for the NVTIA ternary system

3.4. Selected Published Evidence Relevant To Translation

Table 3. Published evidence relevant to the translational interpretation of the ternary system.

Published source	Design	Key data relevant to the ternary system
Badmaev et al., 2000	Double-blind human study	120 mg CoQ10 + 5 mg piperine for 21 days produced an approximately 30% greater plasma AUC than CoQ10 + placebo.
Mortensen et al., 2014 (Q-SYMBIO)	Randomized double-blind trial, 420 patients	MACE 15% vs 26%; cardiovascular mortality 9% vs 16%; all-cause mortality 10% vs 18% with CoQ10 vs placebo.
Xu et al., 2024	Meta-analysis of 33 randomized trials	All-cause mortality RR 0.64; heart-failure hospitalization RR 0.50; 6-min walk distance +31.70 m; BNP and NYHA class improved.
Li & Kopec, 2024	Formulation study	MCT/phospholipid encapsulation increased CoQ10 bioaccessibility 1.4× and Caco-2 uptake 5.5–6.0× versus control.
Mantle & Dybring, 2020	Bioavailability review	Insufficient initial crystal dispersion can reduce CoQ10 bioavailability by about 75%; lipid-based and solubilized formulations are therefore critical.

4. DISCUSSION

The available preclinical dataset suggests that the NVTIA ternary strategy does more than simply increase plasma exposure. All three embodiments outperformed the binary comparator in plasma total CoQ10, yet the gain in myocardial reduced CoQ10 was proportionally larger, especially in the 100:15:1 soft capsule. This pattern is consistent with the proposed relay mechanism: piperine improves upstream entry into the systemic circulation, while vitamin E participates in the downstream antioxidant network that favors maintenance of reduced CoQ10 in target tissue.

Published evidence strengthens the plausibility of each module separately. Piperine has already been shown in a double-blind human study to increase CoQ10 plasma exposure by approximately 30% after 21 days of coadministration [5]. CoQ10 formulation science has also advanced in a direction highly consistent with the current platform; recent studies show that medium-chain-triglyceride and phospholipid encapsulation increases CoQ10 bioaccessibility by 1.4-fold and Caco-2 uptake by 5.5- to 6.0-fold, while broader reviews identify SEDDS, micelles, liposomes, and nanoemulsions as rational approaches for this molecule [3, 4].

The cardiovascular relevance of improving CoQ10 delivery is supported by human outcomes data. In the Q-SYMBIO trial, long-term CoQ10 supplementation reduced major adverse cardiovascular events from 26% to 15% and all-cause mortality from 18% to 10% in chronic heart failure [6]. A 2024 meta-analysis of 33 randomized trials further reported lower all-cause mortality, fewer hospitalizations for heart failure, improved NYHA class, lower BNP, and a longer six-minute walk distance with CoQ10 compared with control [8].

At the same time, our interpretation should remain measured. The public clinical literature supports CoQ10 as a cardiovascular adjunct and supports piperine and formulation engineering as exposure-enhancing tools, but it does not yet prove that this exact ternary ratio delivers superior clinical benefit in humans. The present work therefore supports progression to pharmacokinetic bridging and randomized clinical validation rather than definitive efficacy claims.

5. CONCLUSION

In summary, the NVTIA CoQ10–BioPerine®–vitamin E ternary system presents a ratio-defined, mechanistically coherent platform for improving oral delivery and myocardial redox support. The available preclinical dataset shows stronger myocardial enrichment of reduced CoQ10 than a binary CoQ10–piperine reference, while the published literature independently supports the relevance of piperine, advanced lipid-based formulation strategies, and CoQ10 in chronic heart failure. The next decisive step is clinical confirmation of the exact ternary design in humans.

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