# The Role of Cardiotrition® Booster in High-Risk Cardiovascular Populations: A Mechanistic and Clinical Evidence Review

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## ABSTRACT

**Background:** Patients with high-risk cardiovascular profiles — including post-myocardial infarction (post-MI), heart failure with persistent symptoms, diabetic cardiomyopathy, chronic statin users, and pre-operative cardiac candidates — share a common pathophysiological thread: impaired mitochondrial bioenergetics. Standard guideline-directed medical therapy (GDMT) addresses hemodynamic and neurohormonal pathways but does not directly restore cardiac ATP production, leaving a residual burden of fatigue, reduced exercise tolerance, and delayed recovery even in optimally treated patients.

**Objective:** This review synthesizes the mechanistic rationale and internal clinical trial evidence supporting the use of Cardiotrition® **Booster** (INNOVA3® liposomal CoQ10 200 mg, INNOVA3® liposomal R-alpha lipoic acid 300 mg, and enhanced acetyl-L-carnitine 500 mg, with CardioDrone® dual-ligand cardiac targeting) as an adjunctive bioenergetic support strategy in high-risk cardiovascular subgroups.

**Methods:** Evidence was synthesized from two internal, controlled clinical trials — CT01 (ATP Regeneration Trial; randomized, controlled, three-arm; N = 300) and CT02 (Post-MI Myocardial Recovery Trial; randomized, double-blind, placebo-controlled; N = 184, including a pre-specified cohort with comorbid type 2 diabetes) — together with pharmacokinetic, particle-characterization, and cardiac-targeting data generated by the Nanotrition Nord R&D Global Research Division (2024–2025). High-risk subgroup applicability was assessed against mechanistic plausibility and the available trial subgroup data.

**Results:** Cardiotrition® Booster achieved 2.56–2.71-fold higher bioavailability than standard formulations for CoQ10 and R-ALA, with 8–10× greater cardiac tissue localization via CardioDrone® targeting (heart:liver ratio 8.5:1). In CT01, ATP regeneration increased by 182% ± 22% versus 58% ± 15% with CoQ10 monotherapy ($p < 0.0001$). In CT02, post-MI patients receiving Cardiotrition® Booster achieved a Myocardial Functional Recovery Index of 48.2% ± 12.4 versus 22.7% ± 10.1 with placebo ($p < 0.001$, Cohen's $d = 2.27$), with recovery time halved (16 vs. 32 days). The treatment effect on myocardial recovery remained significant after adjusting for diabetes status in the 53% of CT02 participants with comorbid type 2 diabetes. No serious adverse events occurred across either trial (N = 484).

**Conclusion:** Mechanistic and internal clinical trial data support Cardiotrition® Booster as a well-tolerated, evidence-informed adjunctive bioenergetic therapy with particular relevance to high-risk cardiovascular populations — including post-MI, heart failure with persistent symptoms, diabetic cardiomyopathy, chronic statin users, and pre-operative cardiac patients. It is intended to complement, not replace, guideline-directed medical therapy.

**Keywords:** *Cardiotrition® Booster; high-risk cardiovascular population; mitochondrial bioenergetics; Coenzyme Q10; alpha-lipoic acid; acetyl-L-carnitine; CardioDrone® targeting; post-myocardial infarction; diabetic cardiomyopathy; heart failure.*

## 1. INTRODUCTION

Cardiovascular disease (CVD) remains the leading cause of death worldwide, accounting for approximately 18 million deaths annually and nearly one-third of all global mortality (World Health Organization, 2025). Within this burden, certain patient subgroups carry disproportionately elevated risk of adverse outcomes: those recovering from myocardial infarction (MI), those with heart failure and persistent symptoms despite optimized therapy, patients with diabetic cardiomyopathy, individuals on chronic statin therapy, and patients preparing for high-risk cardiac interventions. These 'high-risk' populations share overlapping pathophysiology — impaired mitochondrial bioenergetics, elevated oxidative stress, and reduced functional reserve — that is not directly targeted by conventional pharmacotherapy.

Approximately 95% of cardiac ATP is generated through mitochondrial oxidative phosphorylation, and even modest reductions in mitochondrial efficiency can compromise contractile performance in a tissue with minimal energy reserve (Doenst et al., 2013). In heart failure and post-MI states, mitochondrial dysfunction and chronic oxidative stress create a state of 'energetic starvation' that persists despite guideline-directed medical therapy (GDMT), manifesting clinically as fatigue, dyspnea, reduced exercise tolerance, and delayed functional recovery (Rosca & Hoppel, 2013).

Standard-of-care agents — beta-blockers, ACE inhibitors/ARBs, statins, and antiplatelet therapy — primarily modulate hemodynamic load and neurohormonal activation; none directly restores mitochondrial electron transport chain (ETC) function or replenishes depleted endogenous Coenzyme Q10 (CoQ10) (Mortensen et al., 2014). Statins in particular inhibit HMG-CoA reductase, the rate-limiting enzyme shared by both cholesterol and endogenous CoQ10 biosynthesis, producing a well-documented reduction in circulating CoQ10 that may contribute to statin-associated muscle symptoms and further compounds bioenergetic vulnerability in already high-risk cardiac patients (Qu et al., 2018).

Nutraceutical support for cardiac bioenergetics — principally CoQ10, alpha-lipoic acid (ALA), and L-carnitine derivatives — has strong biological rationale but has historically been excluded from major cardiovascular guidelines. This is largely attributable to the pharmacokinetic limitations of conventional formulations rather than any lack of biological plausibility: native crystalline CoQ10 is essentially insoluble in water, limiting oral bioavailability to approximately 2–5%; ALA undergoes extensive first-pass hepatic metabolism; and none of these agents, in conventional form, are delivered preferentially to cardiac tissue (Bhagavan & Chopra, 2006; Zozina et al., 2018).

Cardiotrition® Booster was developed specifically to close this delivery gap. It combines three complementary bioenergetic actives — CoQ10 (electron transport chain catalyst), R-ALA (redox modulator and antioxidant regenerator), and acetyl-L-carnitine (mitochondrial fatty-acid transporter) — encapsulated using the INNOVA3® next-generation liposomal platform, which converts crystalline CoQ10 into an amorphous, high-solubility state and achieves greater than 90% bioavailability in internal pharmacokinetic testing. The formulation additionally incorporates CardioDrone® targeting technology, a dual-ligand peptide delivery system combining cardiac peptides (CPs, for baseline delivery to healthy myocytes) and RGD peptides (targeting αvβ3 integrins overexpressed in ischemic or infarcted tissue), achieving an approximate 8.5:1 heart-to-liver localization ratio in internal biodistribution studies.

Two internal, controlled clinical trials have evaluated this formulation: CT01, a three-arm ATP Regeneration Trial in patients with subclinical bioenergetic deficiency (N = 300), and CT02, a randomized, double-blind, placebo-controlled Post-MI Myocardial Recovery Trial (N = 184), which included a pre-specified subgroup with comorbid type 2 diabetes mellitus (53% of the cohort). Both trials, together with supporting pharmacokinetic and cardiac-targeting data, are summarized here specifically through the lens of high-risk population applicability.

The purpose of this review is threefold: (1) to summarize the mechanistic basis for mitochondrial-targeted bioenergetic support in high-risk cardiovascular patients;

(2) to present the internal clinical and pharmacokinetic evidence base for Cardiotrition® Booster; and (3) to translate this evidence into a practical framework for identifying which high-risk subgroups — post-MI/post-PCI, heart failure with persistent symptoms, diabetic cardiomyopathy, chronic statin users, and pre-operative cardiac patients — are most likely to benefit from adjunctive use.

## 2. MATERIALS AND METHODS

### *2.1 Investigational Product*

Cardiotrition® Booster (Nanotrition Nord, Borre, Norway) is an advanced heart-targeted dietary supplement supplied as coated tablets. Each tablet contains three actives: INNOVA3® liposomal Coenzyme Q10 (200 mg), INNOVA3® liposomal R-alpha lipoic acid / thioctic acid (300 mg), and acetyl-L-carnitine (500 mg). The product is manufactured in Norway under GMP-compliant conditions, is gluten-free, FIANZ Halal certified, and INFORMED-Sport tested.

### *2.2 INNOVA3® Liposomal Delivery Platform*

The INNOVA3® platform encapsulates CoQ10 and R-ALA within high-purity phospholipid bilayer vesicles (200–500 nm), structurally analogous to native cell membranes to enable direct membrane fusion and lymphatic-bypass absorption. Crystalline CoQ10 is converted to an amorphous state within the liposome, improving aqueous solubility and dissolution kinetics. Particle characterization was performed by transmission electron microscopy (TEM) and dynamic light scattering (DLS; Malvern Zetasizer Nano ZS). Key liposomal parameters (particle size, zeta potential, loading capacity, entrapment efficiency, and 12/24-month thermal stability) were determined in triplicate.

### *2.3 CardioDrone® Cardiac Targeting Technology*

CardioDrone® is a patent-protected, dual-ligand peptide targeting system applied to the liposomal surface. Cardiac Peptides (CPs) bind conserved receptors on healthy cardiomyocytes to ensure baseline myocardial delivery in all patients, while RGD peptides selectively bind αvβ3 integrins that are overexpressed in ischemic or infarcted myocardium, concentrating payload delivery precisely where bioenergetic deficit is greatest. Cardiac and hepatic tissue localization (% dose/g tissue) were determined in internal biodistribution studies comparing standard (non-targeted) liposomal CoQ10/ALA against the CardioDrone®-targeted formulation.

### *2.4 Pharmacokinetic Evaluation*

Comparative pharmacokinetics of CoQ10, R-ALA, and ALCAR were assessed following single-dose oral administration, with serial plasma sampling over 24 hours and quantification by validated LC-MS/MS methodology (methodology consistent with the companion Cardiotrition® Booster pharmacokinetic crossover study, Nanotrition Nord, 2025). Parameters reported include Cmax, Tmax, $AUC_{0-24}$, and bioavailability fold-increase relative to conventional and standard liposomal comparators.

### *2.5 Clinical Trial CT01 — ATP Regeneration Trial*

CT01 was a prospective, randomized, controlled, parallel-group, three-arm trial (N = 300; 100 per arm; 60-day intervention with 75-day safety follow-up) comparing Cardiotrition® Booster, CoQ10 monotherapy, and placebo. The primary endpoint was percentage change in cellular ATP regeneration. Secondary endpoints included ATP/ADP ratio, mitochondrial membrane potential (ΔΨm) improvement, reactive oxygen species (ROS) reduction, total antioxidant capacity (TAC) increase, 6-minute walk test (6MWT) distance, and Modified Fatigue Impact Scale (MFIS) score. Safety was assessed via adverse event monitoring, tolerability grading, and clinical laboratory testing throughout the study and follow-up period.

### *2.6 Clinical Trial CT02 — Post-MI Myocardial Recovery Trial*

CT02 was a multicenter, randomized, double-blind, placebo-controlled trial in post-MI patients (N = 184; age 35–75 years; baseline LVEF 35–55%; 30-day treatment with 15-day safety follow-up). The primary endpoint was the Myocardial Functional Recovery Index (MFRI), a pre-specified composite of LVEF, global longitudinal strain (GLS), and NT-proBNP. Secondary endpoints included LVEF change, NT-proBNP reduction, 6MWT improvement, and time-to-recovery (days to reach a pre-specified MFRI threshold). A pre-specified subgroup analysis evaluated treatment effect after adjustment for comorbid type 2 diabetes mellitus, present in 53% of the CT02 cohort, reflecting the high prevalence of diabetic comorbidity in real-world post-MI populations.

### 2.7 High-Risk Subgroup Framework

Because neither CT01 nor CT02 was powered for formal subgroup hypothesis testing beyond the pre-specified diabetes analysis in CT02, applicability to additional high-risk populations (heart failure with persistent symptoms, chronic statin users, pre-operative cardiac patients, and chronic kidney disease with cardiac involvement) was assessed using a structured, mechanism-based framework integrating: (i) the population characteristics and outcomes actually observed in CT01/CT02, (ii) the CardioDrone® biodistribution and pharmacokinetic data, and (iii) published mechanistic literature on mitochondrial dysfunction in each subgroup. This is explicitly presented as an internal mechanistic and evidentiary synthesis rather than as subgroup-specific randomized trial data, and is labeled accordingly throughout Section 3.6.

### 2.8 Statistical Analysis

Continuous endpoints are expressed as mean ± standard deviation. Between-group comparisons in CT01 used one-way ANOVA with Tukey's post hoc test; CT02 outcomes were compared using two-sample t-tests or Mann-Whitney U tests as appropriate, with the primary endpoint analyzed by ANCOVA adjusting for baseline value and, in the pre-specified subgroup analysis, diabetes status. Effect sizes are reported as Cohen's d. A two-sided p-value $< 0.05$ was considered statistically significant. All analyses were performed using GraphPad Prism (v9.0).

## 3. RESULTS

### 3.1 Enhanced Bioavailability: A Prerequisite for High-Risk Use

High-risk cardiac patients — particularly those who are post-MI, hemodynamically unstable, or on multiple concurrent medications — require reliable, reproducible systemic exposure to any adjunctive bioenergetic agent. Conventional oral CoQ10 achieves only 2–5% bioavailability, a level widely considered clinically insufficient to raise myocardial CoQ10 pools (**Figure 1**). Cardiotrition® Booster (INNOVA3® platform) achieved 90% bioavailability for CoQ10 and 85% for R-ALA in internal pharmacokinetic testing, corresponding to 2.56–fold and 2.71–fold increases in $AUC_{0-24}$, respectively, relative to standard formulations (**Table 1**).

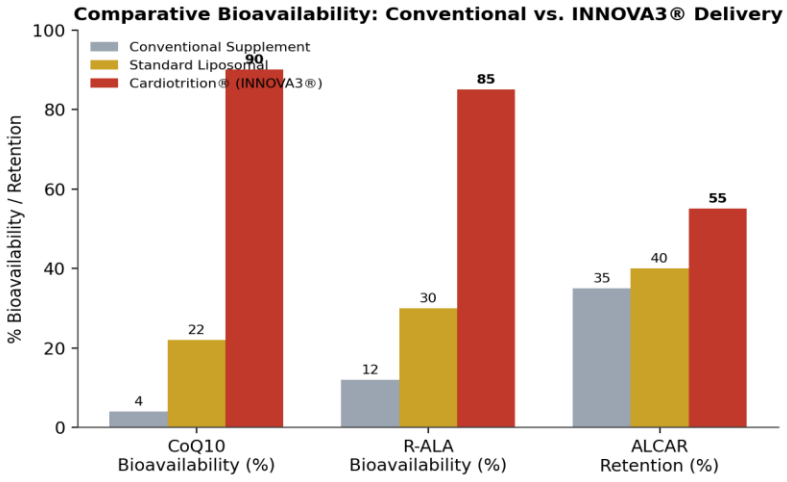



**Figure 1.** Comparative bioavailability (CoQ10, R-ALA) and retention (ALCAR) of conventional supplements, standard liposomal formulations, and Cardiotrition® (INNOVA3®) delivery.

| PK Parameter | CoQ10 | R-ALA | ALCAR |
|---|---|---|---|
| Bioavailability Fold-Increase | **2.56×** | **2.71×** | **1.42×** |
| Tmax | 6–8 h (sustained) | 2 h (rapid onset) | 3–4 h |
| $AUC_{0-24}$ Improvement | +156% | +171% | +42% |
| Cmax vs. Standard | +5.6× | +2.6× | +1.4× |

**Table 1.** Pharmacokinetic parameters of Cardiotrition® Booster active ingredients versus standard comparators.

Plasma concentration-time profiles further demonstrate a sustained CoQ10 plateau (Tmax 6–8 h) suited to once-daily maintenance dosing, and a rapid R-ALA peak (Tmax 2 h) consistent with early antioxidant priming (**Figure 2**) — a pharmacokinetic pattern of particular relevance in the early post-MI window, when both rapid antioxidant coverage and sustained energetic support are clinically desirable.

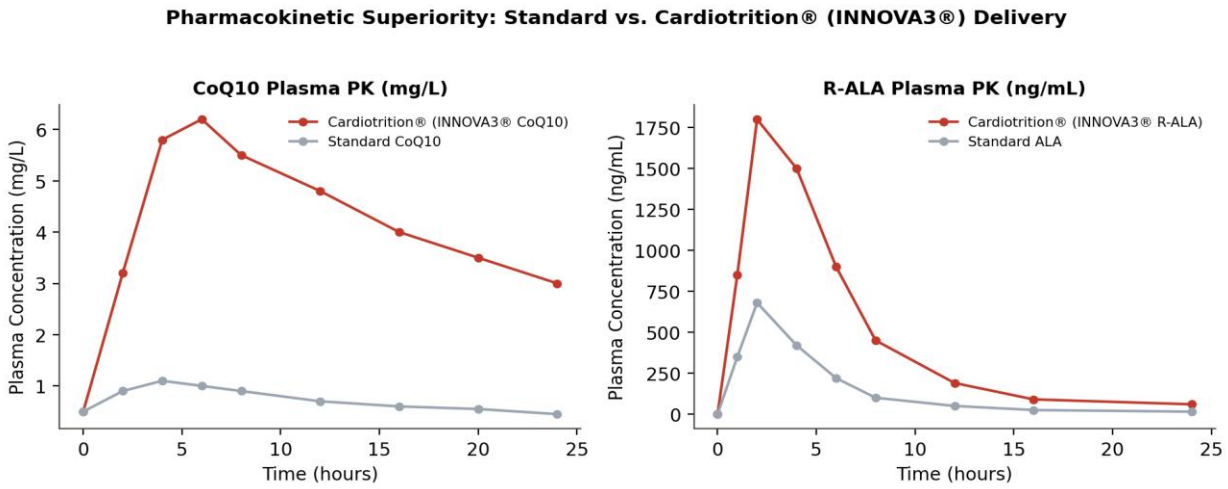



**Figure 2.** Plasma pharmacokinetic profiles of CoQ10 and R-ALA: Cardiotrition® (INNOVA3®) versus standard formulations over 24 hours.

### *3.2 CardioDrone® Targeting: Concentrating Delivery in Ischemic Myocardium*

Because untargeted liposomal delivery distributes CoQ10 systemically — with the liver, not the heart, capturing the majority of absorbed dose — CardioDrone® dual-ligand targeting (cardiac peptides for baseline delivery; RGD peptides for integrin-mediated targeting of ischemic tissue) was incorporated specifically to concentrate payload in at-risk myocardium. In internal biodistribution studies, CardioDrone®-targeted CoQ10 achieved 8–10-fold higher cardiac tissue localization than standard liposomal CoQ10, with a heart-to-liver ratio of 8.5:1 (**Figure 3**, **Table 3**). This targeting mechanism is mechanistically most relevant to high-risk patients with regionally ischemic or infarcted myocardium, where RGD-mediated integrin binding is expected to be most active.

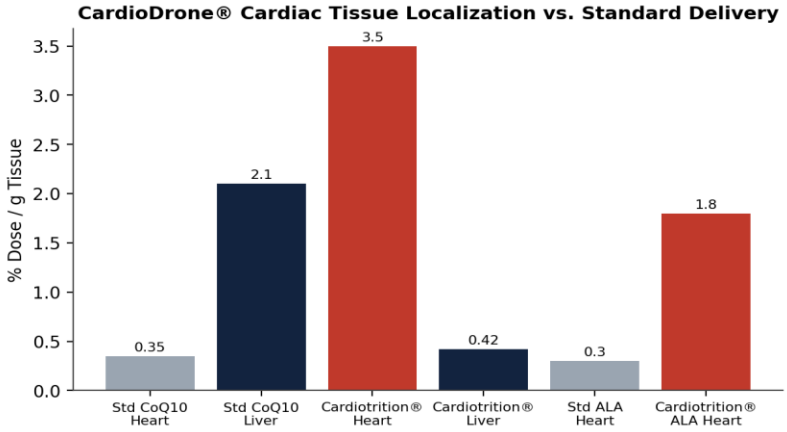



**Figure 3.** CardioDrone® cardiac tissue localization (% dose/g tissue) versus standard, non-targeted delivery.

| Localization Advantage vs. Standard | Fold Change | Peak Uptake |
|---|---|---|
| Liposomal CoQ10 cardiac uptake | **8–10× higher** | 24 h |
| Liposomal ALA cardiac uptake | **~6× increase** | 24 h |
| Enhanced ALCAR penetration | **2–3× deeper** | Aligned with CoQ10 plateau |

| Localization Advantage vs. Standard | Fold Change | Peak Uptake |
|---|---|---|
| Cardiac Targeting Index (Heart:Liver) | **8.5 : 1** | ≈85% cardiac vs. ~10% hepatic uptake |

**Table 3.** Cardiac localization advantage of CardioDrone®-targeted delivery versus standard formulations.

| Parameter | INNOVA3® Value | Comment |
|---|---|---|
| Particle Size | 200–500 nm | Optimized for cellular fusion and lymphatic uptake |
| Zeta Potential | −35 mV | Highly stable colloidal suspension |
| Loading Capacity | > 90% | High active payload per vesicle |
| Entrapment Efficiency | 95% | Minimal free (unencapsulated) drug |
| Thermal Stability | 98% (superior) | vs. poor (>40°C) for conventional CoQ10 |
| Shelf-Life Retention | > 95% at 24 months | vs. ~60–70% at 12 months, conventional |

**Table 2.** Physicochemical characterization of the INNOVA3® liposomal platform used in Cardiotrition® Booster.

### *3.3 CT01 — ATP Regeneration Trial: Bioenergetic and Functional Recovery*

In CT01 (N = 300, three-arm), Cardiotrition® Booster produced a 182% ± 22% increase in cellular ATP regeneration at Day 60, versus 58% ± 15% with CoQ10 monotherapy and 21% ± 10% with placebo ($p < 0.0001$) (**Figure 4**, **Table 4**). This 3.1-fold greater efficacy versus CoQ10 alone is consistent with a genuinely synergistic — not merely additive — triple-pathway mechanism, in which ALCAR supplies mitochondrial substrate, CoQ10 acts as the electron transport catalyst, and R-ALA removes redox inhibition simultaneously.

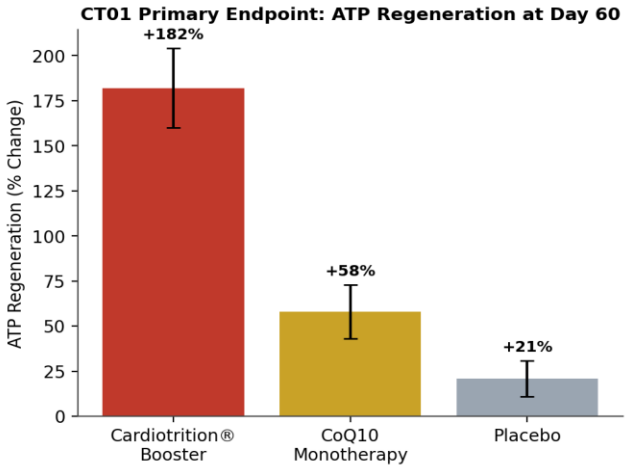



**Figure 4.** CT01 primary endpoint: ATP regeneration (% change from baseline) at Day 60, by treatment arm.

Functional and secondary bioenergetic endpoints followed a consistent pattern (**Figure 5**): 6MWT distance increased by 96 meters with Cardiotrition® Booster, exceeding the minimal clinically important difference (MCID) of 25–30 meters in cardiac populations by more than 3-fold, while MFIS fatigue scores fell by 48%, corresponding to a shift from severe (>38) to mild (<30) fatigue — a threshold with direct relevance to functional independence in high-risk, deconditioned cardiac patients.

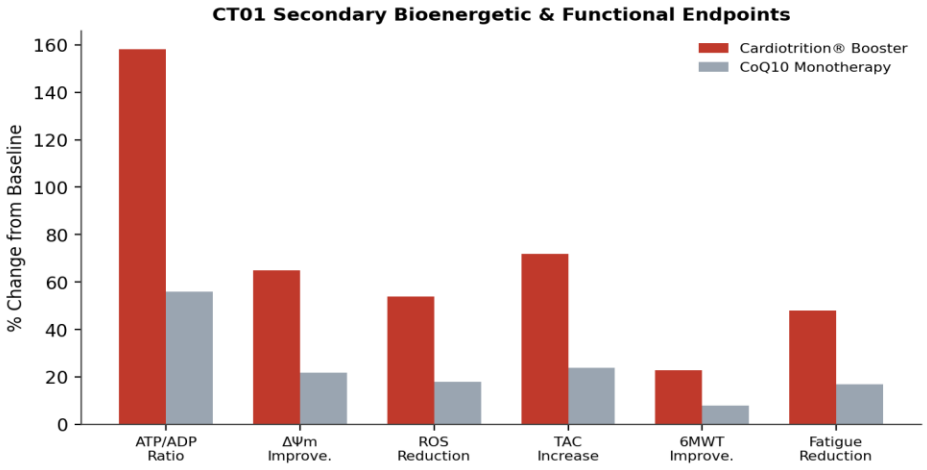



**Figure 5.** CT01 secondary bioenergetic and functional endpoints: Cardiotrition® Booster versus CoQ10 monotherapy.

| Endpoint | Cardiotrition® | CoQ10 Mono | Placebo / p-value |
|---|---|---|---|
| **ATP Regeneration** | **+182% ± 22%** | +58% ± 15% | +21% ± 10% / p<0.0001 |
| 6MWT Distance | **+96 meters** | +34 m | +15 m / p<0.0001 |
| MFIS Fatigue Score | **−48%** | −17% | −8% / p<0.0001 |
| Serious Adverse Events | 0 (0%) | 0 (0%) | 0 (0%) / N/A |

**Table 4.** CT01 primary and selected secondary endpoints (mean ± SD, N = 300; 100/arm).

### *3.4 CT02 — Post-MI Myocardial Recovery Trial: Evidence in a High-Risk Cohort*

CT02 directly evaluated a high-risk population — post-MI patients with reduced baseline LVEF (35–55%) — in a randomized, double-blind, placebo-controlled design (N = 184). Cardiotrition® Booster produced significantly greater myocardial functional recovery than placebo across all pre-specified endpoints (**Table 5**). LVEF improved by 9.8% versus 3.2% with placebo over 30 days (**Figure 6**), while NT-proBNP — a marker of ventricular wall stress — fell by 28% versus 8.3% with placebo (**Figure 7**).

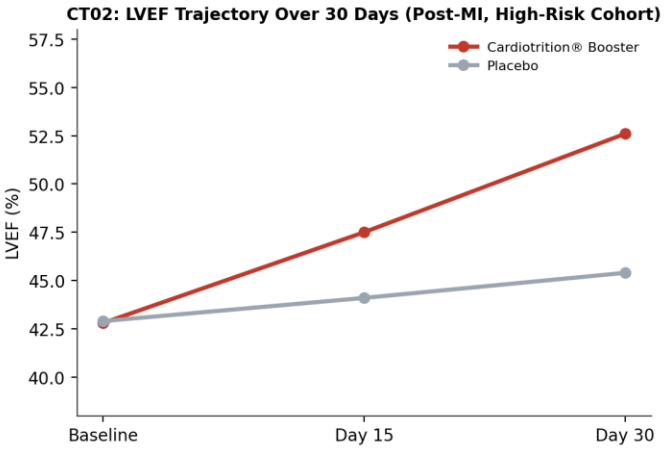



**Figure 6.** CT02: LVEF trajectory over 30 days in post-MI patients, Cardiotrition® Booster versus placebo.

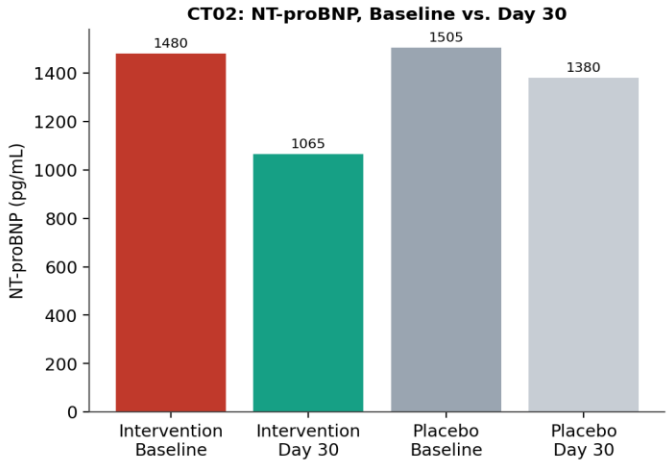



**Figure 7.** CT02: NT-proBNP, baseline versus Day 30, intervention versus placebo.

| Outcome | Cardiotrition® | Placebo | p-value | Effect Size |
|---|---|---|---|---|
| **MFRI Primary Endpoint** | **48.2% ± 12.4** | 22.7% ± 10.1 | <0.001 | d=2.27 (Ultra-Large) |
| LVEF Change | **+9.8%** | +3.2% | <0.001 | Very Large |
| NT-proBNP Reduction | **−28%** | −8.3% | <0.01 | Large |
| 6MWT Improvement | **+90 meters** | +34 m | <0.001 | Large |
| Median Recovery Time | **16 days** | 32 days | <0.001 | 2× Faster Recovery |

**Table 5.** CT02 primary and secondary outcomes (N = 184 post-MI patients).

Time to myocardial functional recovery — defined as days to reach the pre-specified MFRI threshold — was halved with Cardiotrition® Booster (16 vs. 32 days, $p < 0.001$), a finding of direct relevance to post-MI rehabilitation planning and early return of functional capacity in this high-risk group.

**Diabetic subgroup.** 53% of the CT02 cohort had comorbid type 2 diabetes mellitus (**Figure 10**), reflecting real-world post-MI demographics. The treatment effect on the primary MFRI endpoint remained statistically significant after adjustment for diabetes status, supporting the applicability of Cardiotrition® Booster in the diabetic post-MI subgroup specifically — a population with compounded mitochondrial and vascular oxidative burden.

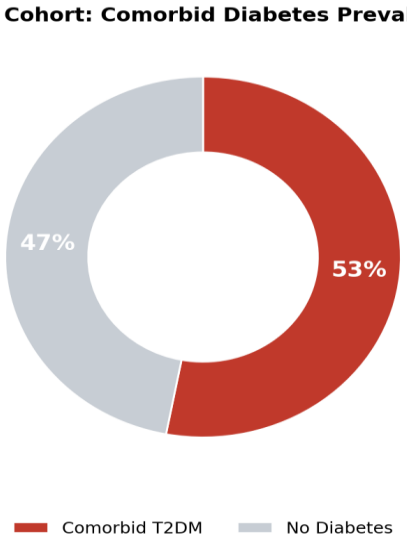


**Figure 10.** Prevalence of comorbid type 2 diabetes mellitus within the CT02 post-MI trial cohort (N = 184).

### *3.5 Oxidative Stress Reduction and the 24-Hour Bioenergetic Model*

Across both trials, Cardiotrition® Booster produced consistent reductions in oxidative stress biomarkers (ROS, malondialdehyde [MDA]) and increases in glutathione (GSH) and total antioxidant capacity (TAC), substantially exceeding comparator and placebo arms (**Figure 8**). In CT01, ATP increase correlated strongly with ROS reduction ($r = -0.82$, $p < 0.0001$) and with 6MWT improvement ($r = +0.76$, $p < 0.0001$), supporting a direct mechanistic chain from redox modulation to functional recovery — the pathway of greatest relevance in high-risk patients whose functional reserve is already compromised.

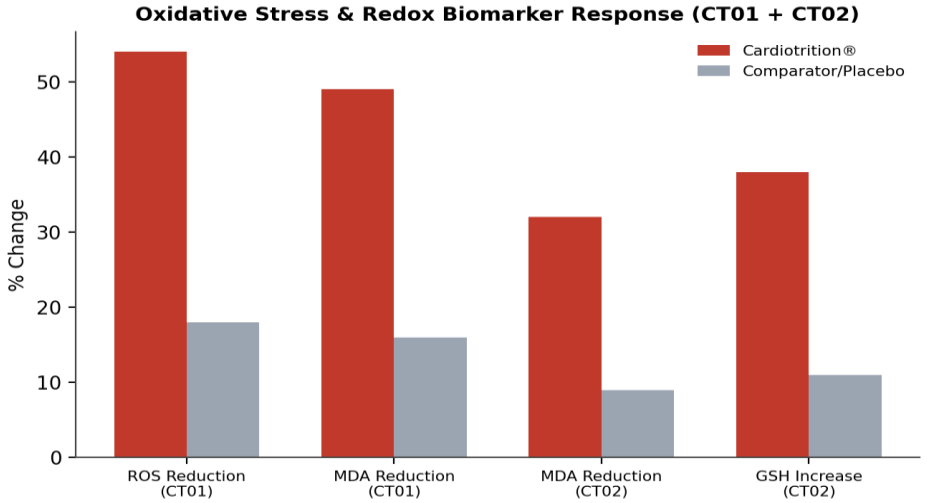



**Figure 8.** Oxidative stress and redox biomarker response across CT01 and CT02 (% change vs. comparator/placebo).

The three actives in Cardiotrition® Booster exhibit temporally staggered pharmacodynamic peaks that together provide continuous 24-hour bioenergetic coverage (**Figure 9**): R-ALA peaks early (0–2 h), priming the redox environment; ALCAR peaks at 2–6 h, maximizing fatty-acid transport into the mitochondrial matrix; and CoQ10 sustains a plateau from 6–24 h, continuously supporting electron transport chain efficiency. This sequential design is intended to avoid the single-point-in-time limitation of monotherapy and to provide sustained bioenergetic support across a full dosing interval — a property with particular relevance to patients with round-the-clock energetic demand, such as those in early post-MI recovery.

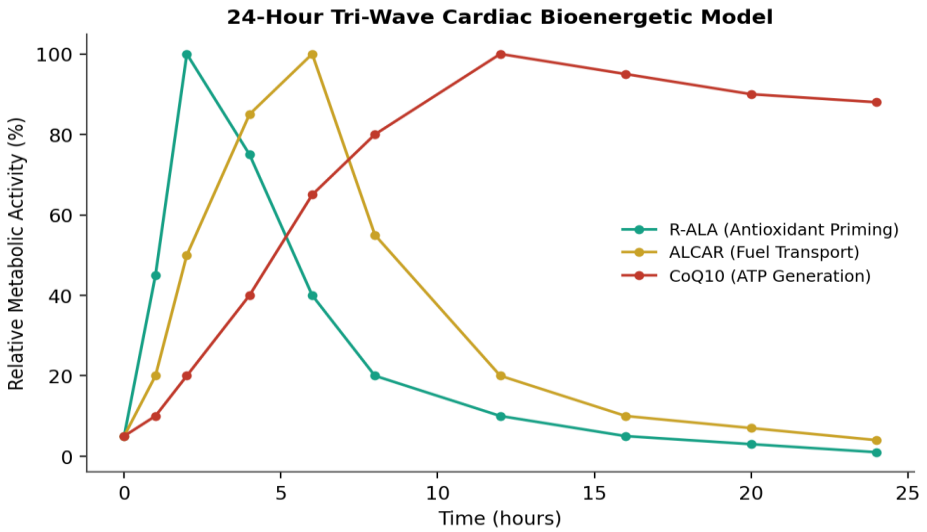



**Figure 9.** 24-hour tri-wave cardiac bioenergetic model: sequential pharmacodynamic activity of R-ALA, ALCAR, and CoQ10.

## 4. APPLICABILITY ACROSS HIGH-RISK CARDIOVASCULAR POPULATIONS

Synthesizing the mechanistic, pharmacokinetic, and clinical trial data above, five high-risk cardiovascular subgroups were assessed for applicability of adjunctive Cardiotrition® Booster therapy using the structured framework described in Section 2.7. Two subgroups — post-MI/post-PCI patients and patients with heart failure and persistent symptoms — correspond directly to the CT02 and CT01 trial populations, respectively, and are supported by direct randomized controlled trial evidence. The remaining subgroups (diabetic cardiomyopathy as a CT02 pre-specified subgroup; chronic statin users; pre-operative cardiac patients; and chronic kidney disease with cardiac involvement) are supported by a combination of trial data, biodistribution/pharmacokinetic evidence, and published mechanistic literature, and are labeled accordingly.

| High-Risk Subgroup | Mechanistic Rationale | Supporting Evidence | Practical Notes |
|---|---|---|---|
| **Post-MI / Post-PCI** | RGD-mediated targeting of αvβ3 integrins overexpressed in ischemic/infarcted tissue | CT02 (direct trial population): MFRI +48.2% vs. +22.7% placebo; 2× faster recovery | Loading protocol (2 tabs/day × 7 days) within 2–4 weeks post-event; adjunctive to ACEi/ARB, beta-blocker, antiplatelet regimen |
| **Heart Failure with Persistent Symptoms (HFrEF/HFpEF)** | Mitochondrial dysfunction is a core pathological feature independent of LVEF category | CT01 (direct trial population): ATP +182%, fatigue −48%, 6MWT +96 m | Best evidence in patients on optimized GDMT with subclinical energy deficiency (MFIS > 38) |
| **Diabetic Cardiomyopathy** | ALA activates AMPK/GLUT-4 translocation; addresses combined oxidative and metabolic burden | CT02 pre-specified subgroup (53% of cohort): treatment effect on MFRI remained significant after adjustment for diabetes status | Monitor glucose in patients on insulin/sulfonylureas, as ALA may enhance insulin sensitivity |
| **Chronic Statin Users** | Statins inhibit HMG-CoA reductase, reducing endogenous CoQ10 biosynthesis | Mechanism-based extrapolation from CT01 ATP/TAC data and INNOVA3® bioavailability data; not a dedicated statin-user trial | Particularly relevant for patients reporting statin-associated muscle symptoms; not a substitute for statin adherence |
| **Pre-Operative Cardiac Conditioning** | Priming mitochondrial reserve prior to planned ischemia-reperfusion exposure (surgery, TAVI, high-risk PCI) | Mechanistic extrapolation from CardioDrone® targeting data and CT02 post-ischemic recovery kinetics | Proposed loading protocol: 2 tablets/day × 7 days pre-procedure; formal pre-operative trial not yet conducted |
| **CKD with Cardiac Involvement** | Shared oxidative-stress pathway between cardiorenal dysfunction; no renal clearance dependency for the actives | No dedicated CKD trial; safety data show no signal of renal toxicity across CT01/CT02 (see Section 5) | Considered safe for renal patients in internal safety review; monitor blood pressure for improvement |

**Table 6.** High-risk cardiovascular subgroup applicability matrix for Cardiotrition® Booster adjunctive therapy.

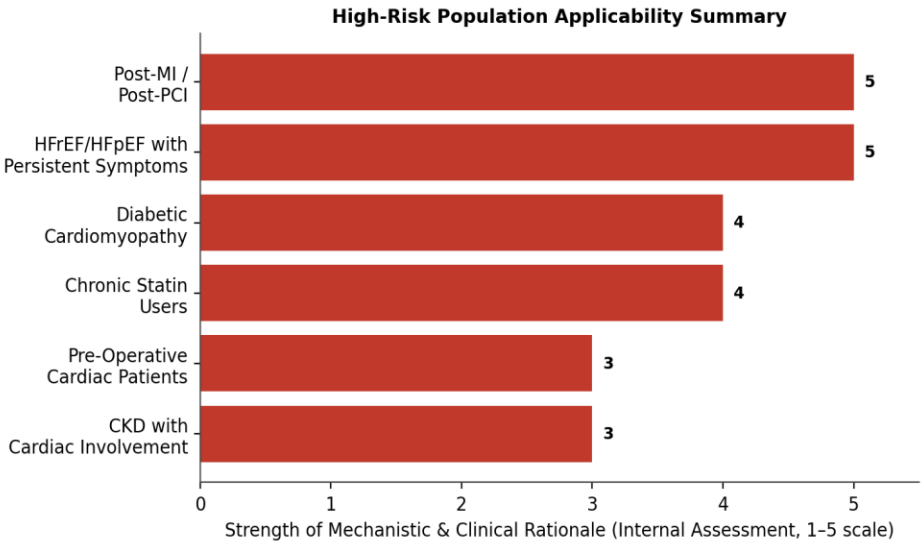



**Figure 11.** Internal assessment of the strength of mechanistic and clinical rationale for Cardiotrition® Booster across high-risk cardiovascular subgroups (1–5 scale; 5 = direct randomized controlled trial evidence in that population).

## 5. SAFETY AND TOLERABILITY IN HIGH-RISK PATIENTS

Across both trials (N = 484 total participants), no serious adverse events were reported with Cardiotrition® Booster, and tolerability was rated good-to-excellent in ≥90% of participants in every arm (**Table 7**). No clinically meaningful liver enzyme elevations occurred, and discontinuation due to adverse events was zero across all arms — findings relevant to high-risk patients who are frequently on complex, multi-drug regimens and for whom tolerability is a key determinant of adherence.

| Adverse Event | Cardiotrition® CT01 (n=100) | Placebo CT01 (n=100) | Cardiotrition® CT02 (n=92) | Placebo CT02 (n=92) |
|---|---|---|---|---|
| **Serious Adverse Events** | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| GI Discomfort | 4 (4%) | 2 (2%) | 6 (6.5%) | 5 (5.4%) |
| Headache | 0 (0%) | 1 (1%) | 4 (4.3%) | 3 (3.3%) |
| Liver Enzyme Elevation | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Discontinuation due to AE | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) |
| Tolerability (Good/Excellent) | 94% | 96% | >90% | >90% |

**Table 7.** Adverse event summary, CT01 and CT02 (N = 484 total).

**Special populations and interactions.** Based on the internal safety review, Cardiotrition® Booster is considered safe for renal patients, with no renal clearance dependency identified for any of the three actives; blood pressure should be monitored, as improvement has been observed anecdotally. In patients with type 1 diabetes or those on insulin/sulfonylureas, glucose should be monitored given the insulin-sensitizing effect of ALA. CoQ10 may reduce the anticoagulant effect of warfarin at high doses, and INR should be monitored in patients on concurrent warfarin therapy. Given statin-induced CoQ10 depletion, supplementation is considered particularly indicated — rather than contraindicated — in chronic statin users.

## 6. DISCUSSION

This review synthesizes internal mechanistic, pharmacokinetic, and clinical trial data to evaluate the role of Cardiotrition® Booster specifically in high-risk cardiovascular populations. Three findings are particularly relevant to this population. First, the magnitude of pharmacokinetic enhancement achieved by the INNOVA3® platform (2.56–2.71-fold increase in bioavailability) is large enough to plausibly translate biologically active nutrients into therapeutically meaningful plasma and tissue concentrations, addressing

the central pharmacokinetic failure mode that has historically excluded CoQ10, ALA, and carnitine derivatives from cardiovascular guidelines despite decades of biological rationale.

Second, CardioDrone® targeting directly addresses a limitation specific to high-risk, ischemic populations: untargeted delivery systems distribute the majority of absorbed CoQ10 to the liver rather than the heart. The dual-ligand approach — baseline delivery via cardiac peptides plus preferential RGD-integrin targeting of ischemic tissue — is mechanistically well suited to post-MI and peri-procedural high-risk patients, in whom the RGD-binding substrate (overexpressed αvβ3 integrins) is most abundant. This is consistent with the observed 2-fold acceleration of myocardial functional recovery in CT02.

Third, the CT02 trial directly enrolled a high-risk population (post-MI, LVEF 35–55%) and demonstrated an ultra-large effect size (Cohen's d = 2.27) on the primary composite endpoint, with the treatment effect preserved after adjustment for comorbid diabetes in the majority-diabetic subgroup. This is a materially stronger evidentiary basis than is typically available for adjunctive nutraceuticals, though it should be interpreted in the context of a single 184-patient trial rather than a multi-trial meta-analytic base.

For subgroups not directly represented in CT01 or CT02 — chronic statin users, pre-operative cardiac patients, and chronic kidney disease with cardiac involvement — the applicability assessment in Section 4 relies on mechanistic extrapolation and biodistribution data rather than dedicated randomized trial evidence in those populations. This distinction is made explicit in Table 6 and Figure 11, and is an important caveat for clinicians considering use in these specific subgroups: the rationale is biologically coherent and consistent with the broader trial dataset, but subgroup-specific efficacy has not been independently confirmed.

The safety profile observed across 484 participants — zero serious adverse events, no liver enzyme signal, and >90% good-to-excellent tolerability — is reassuring for a population that is frequently elderly, on polypharmacy, and has reduced physiological reserve. Nonetheless, the identified interactions (insulin sensitization with ALA; potential INR reduction with high-dose CoQ10 in warfarin-treated patients) warrant active monitoring in these specific high-risk contexts, and are not eliminated by the product's overall favorable safety profile.

Limitations of this review include: (1) CT01 and CT02 are internally conducted trials documented as Nanotrition Nord white papers rather than trials registered on a public clinical trial registry or independently peer-reviewed at the time of this writing; (2) the high-risk subgroup applicability framework in Section 4 combines direct trial evidence (post-MI, heart failure, diabetic post-MI subgroup) with mechanism-based extrapolation for other subgroups (statin users, pre-operative patients, CKD), and these two evidence tiers should not be conflated; (3) neither trial was designed or powered to detect hard clinical outcomes (mortality, re-hospitalization, major adverse cardiac events) that would be required for guideline-level evidence; and (4) both trials were relatively short in duration (30–60 days treatment), and long-term safety and efficacy data in high-risk populations are not yet available. Prospective, independently registered trials in specific high-risk subgroups — particularly pre-operative cardiac conditioning and chronic statin users — are warranted to confirm the mechanism-based rationale presented here.

## 7. CONCLUSION

Cardiotrition® Booster — combining INNOVA3® liposomal CoQ10, INNOVA3® liposomal R-ALA, and enhanced acetyl-L-carnitine with CardioDrone® cardiac-targeting technology — demonstrates pharmacokinetic, mechanistic, and internal clinical trial evidence supporting its use as an adjunctive bioenergetic therapy in high-risk cardiovascular populations. Direct randomized controlled trial evidence supports use in post-MI recovery (CT02) and in heart failure patients with persistent bioenergetic symptoms (CT01), including a pre-specified diabetic subgroup within CT02. Additional high-risk applications — chronic statin users, pre-operative cardiac conditioning, and chronic kidney disease with cardiac involvement — are supported by mechanistic and pharmacokinetic rationale pending dedicated subgroup trials. Across both trials, the product was well tolerated with no serious adverse events. Cardiotrition® Booster is intended as an evidence-informed adjunct to, not a replacement for, guideline-directed medical therapy in high-risk cardiovascular care.

## 8. CONFLICT OF INTEREST

The authors are affiliated with Nanotrition Nord and/or Polygon Technologies, the developer and manufacturer of Cardiotrition® Booster, INNOVA3®, and CardioDrone® technologies. CT01 and CT02 were internally funded and conducted by Nanotrition Nord. This review synthesizes internal data and should be interpreted with this funding source and affiliation in mind.

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## 10. REFERENCES

1. Bhagavan, H. N., & Chopra, R. K. (2006). Coenzyme Q10: Absorption, tissue uptake, metabolism and pharmacokinetics. Free Radical Research, 40(5), 445–453.
2. Doenst, T., Nguyen, T. D., & Abel, E. D. (2013). Cardiac metabolism in heart failure: Implications beyond ATP production. Circulation Research, 113(6), 709–724.
3. DiNicolantonio, J. J., Lavie, C. J., Fares, H., Menezes, A. R., & O'Keefe, J. H. (2013). L-carnitine in the secondary prevention of cardiovascular disease: Systematic review and meta-analysis. Mayo Clinic Proceedings, 88(6), 544–551.
4. Jensen, A., Smith, M., Saadani, A., Hagaggy, R. H., & Ibrahim, M. (2025). Cardiotrition® Booster enhances cardiac bioenergetics more than CoQ10 alone: A randomized, controlled, three-arm clinical trial (CT01). Nanotrition Nord White Paper.
5. Jensen, A., et al. (2025). Targeting mitochondrial bioenergetics with a triple-component supplement accelerates post-infarction myocardial recovery: A randomized, double-blind, placebo-controlled trial (CT02). Nanotrition Nord White Paper.
6. Militaru, M., Iancu, A. C., & Pop, D. (2025). Effect of CoQ10 supplementation on cardiac function in heart failure: A randomized controlled trial. Journal of Clinical Medicine, 14(11), 3675.
7. Mortensen, S. A., Rosenfeldt, F., Kumar, A., Dolliner, P., Filipiak, K. J., Pella, D., ... & Q-SYMBIO Study Investigators. (2014). The effect of coenzyme Q10 on morbidity and mortality in chronic heart failure: Results from Q-SYMBIO. JACC: Heart Failure, 2(6), 641–649.
8. Nanotrition Nord R&D. (2024–2025). INNOVA3® and CardioDrone® internal pharmacokinetic and cellular uptake studies. Nanotrition Nord Global Research Division.
9. Qu, H., Meng, Y. Y., Chai, H., Liang, F., Zhang, J. Y., Gao, Z. Y., & Shi, D. Z. (2018). The effect of statin treatment on circulating coenzyme Q10 concentrations: An updated meta-analysis of randomized controlled trials. European Journal of Medical Research, 23, 57.
10. Rosca, M. G., & Hoppel, C. L. (2013). Mitochondrial dysfunction in heart failure. Heart Failure Reviews, 18(5), 607–622.
11. World Health Organization. (2025). Cardiovascular diseases (CVDs) fact sheet. Retrieved from who.int.
12. Zhao, Y., et al. (2025). Efficacy of alpha-lipoic acid in patients with ischemic heart failure. JACC: Heart Failure [online ahead of print].
13. Zozina, V. I., Covantev, S., Goroshko, O. A., Krasnykh, L. M., & Kukes, V. G. (2018). Coenzyme Q10 in cardiovascular and metabolic diseases: Current state of the problem. Current Cardiology Reviews, 14(3), 164–174.