Keyora Co-Q10 17 in 1

A Multi-Nutrient Synergistic Intervention Program within the "Three-Axis, Seven-Module Framework," Integrating Energy, Antioxidant, Cardiovascular, Neuroprotective, and Anti-Aging Pathways

Abstract

Background: Coenzyme Q10 (CoQ10) has been extensively studied as a mitochondrial cofactor and lipid-soluble antioxidant, yet existing literature often addresses its mechanisms or clinical applications in isolation.

A comprehensive framework integrating its energy-driving role, antioxidant capacity, and systemic disease-intervention value has been lacking.

Objective: This review synthesizes mechanistic, clinical, and formulation-based evidence of CoQ10 within the Keyora *Three-Axis, Seven-Module Framework*, aiming to establish a holistic nutritional paradigm that bridges functional and clinical nutrition.

Methods: We critically examined mechanistic pathways (electron transport chain efficiency, reactive oxygen species regulation, membrane lipid integration, neurotransmitter and enzymatic cofactor interactions), population-based evidence (neurodegenerative diseases, cardiovascular conditions, type II diabetes, cancer patients

undergoing chemotherapy, elderly populations, and dermatological aging), and formulation strategies (bioavailability enhancement via lipid micellization and synergistic cofactors). Data were drawn from randomized controlled trials, cohort studies, mechanistic experiments, and consensus statements.

Results:

- **Axis I – Mitochondrial Energy Axis**: CoQ10 restores ATP production and reduces ROS leakage; Omega-3/6/9 fatty acids (α-linolenic acid (ALA), linoleic acid (LA), oleic acid (OA)) stabilize mitochondrial membranes; vitamins/minerals act as cofactors sustaining energy metabolism.
- **Axis II – Antioxidant and Cellular Protection Axis**: A cross-phase antioxidant network integrates CoQ10, vitamin C/E, selenium, and zinc, with fatty acids optimizing membrane resistance and n-6/n-3 balance.
- **Axis III – Disease Intervention and Anti-Aging Axis**: Evidence supports CoQ10 and nutrient synergy in delaying Alzheimer's and Parkinson's disease, compensating drug-induced nutrient deficiencies (statins, metformin, chemotherapeutics), and protecting skin from aging via collagen synthesis, barrier lipid restoration, and photoaging defense.
- **Formulation strategy**: Bioavailability of CoQ10 is significantly enhanced by co-micellization with poly- and monounsaturated fatty acids and by enzymatic support

from vitamins/minerals, enabling systemic delivery across digestive absorption, plasma circulation, and blood–brain barrier transport.

Conclusions: CoQ10 is not merely a single antioxidant supplement but functions as the central "driving force" within a closed-loop system of *energy-antioxidant-structural-disease-aging* regulation.

The Keyora Co-Q10 17 in 1 formulation exemplifies this integrative approach, demonstrating cross-mechanistic, cross-disease, and cross-population applicability.

This framework redefines CoQ10 as a cornerstone of nutritional pharmacology and a translational bridge between functional and clinical nutrition.

Keywords:

Coenzyme Q10; Mitochondria metabolism; Reactive Oxygen Species metabolism; Antioxidants therapeutic use; Fatty Acids Omega-3 therapeutic use; Fatty Acids Omega-6 therapeutic use; Oleic Acid metabolism; Vitamins pharmacology; Minerals pharmacology; Bioavailability; Alzheimer Disease drug therapy; Parkinson Disease drug therapy; Diabetes Mellitus Type II drug therapy; Neoplasms drug therapy; Chemotherapy-Induced Toxicity prevention and control; Skin Aging drug effects; Nutritional Support; Dietary Supplements; Evidence-Based Medicine.

Modern chronic diseases and aging-related conditions are generally characterized by energy metabolic dysfunction, excessive oxidative stress, persistent inflammatory responses, and multi-system functional decline. While single-nutrient supplementation has received evidence-based support in specific domains - such as the use of coenzyme Q10 in cardiovascular and energy metabolism - its effects are often constrained by insufficient absorption, gaps in metabolic pathways, and unmet systemic demands.

Consequently, the central challenge in nutritional medicine is how to achieve cross-system intervention through synergistic combinations of multiple nutrients.

Keyora Co-Q10 17 in 1 was designed around three core pillars:

- High-dose coenzyme Q10 (250 mg), serving as the driving force for energy metabolism and antioxidant defense
- Omega-3/6/9 fatty acid matrix (734 mg), targeting the common dietary imbalance in the n-6/n-3 ratio while supporting membrane structure and inflammation regulation
- A comprehensive complex of vitamins and minerals (16 essential cofactors), providing metabolic coenzymes and maintaining systemic homeostasis

Building on this foundation, the formulation is systematically structured within the ***Three-Axis, Seven-Module Framework***: from the Mitochondrial Energy Axis (ATP generation and fatigue recovery), to the Antioxidant–Cellular Protection Axis (antioxidant network and cardiovascular endothelial protection), and further to the Disease Intervention - Anti-

Aging Axis (neuro-support, drug-induced deficiency prevention, and skin health).

This design establishes a synergistic intervention model that spans energy, antioxidant defense, cardiovascular protection, neuroprotection, and anti-aging.

Rather than limiting coenzyme Q10 to its standalone effects, this framework provides a closed-loop integration of metabolism and function. By coupling fatty acids with a network of micronutrient cofactors, it achieves a truly systemic nutritional intervention strategy, offering evidence-based support for cardiovascular health, neurological function, exercise performance, and healthy aging.

Keyora Co-Q10 17 in 1 establishes three core pillars in its formulation design:

1) Coenzyme Q10 (250 mg)

Coenzyme Q10 represents the first core pillar of Keyora Co-Q10 17 in 1. It possesses a dual identity as both a key factor in mitochondrial energy metabolism and a central molecule in systemic antioxidant defense. Its unique molecular mechanisms confer an irreplaceable role within the formulation.

Energy Dimension – Coenzyme Q10 functions as an essential electron carrier between Complex I/II and Complex III in the electron transport chain, directly determining the efficiency of ATP synthesis. When Co-Q10 levels decline due to aging, disease, or pharmacological agents such as statins, cells face aggravated energy deficits,

manifested as cardiac weakness, insufficient neuronal energy supply, and reduced exercise endurance. High-dose supplementation (≥200 mg/day) has been shown to significantly enhance cellular energy status and restore metabolic activity.

Antioxidant Dimension – In its reduced form (ubiquinol), Coenzyme Q10 directly scavenges free radicals while regenerating vitamin E and vitamin C, thereby maintaining a closed-loop antioxidant network across both lipid and aqueous compartments. It stabilizes cell membranes and mitochondrial membranes, reduces lipid peroxidation and DNA damage, and thus serves as a core molecule of systemic antioxidant protection and membrane stability.

Systemic Dimension – The effects of Coenzyme Q10 extend across multiple organ systems:

- **Cardiovascular:** Large-scale clinical trials such as Q-SYMBIO and KISEL-10 have demonstrated that high-dose Co-Q10 supplementation reduces the risk of heart failure progression and cardiovascular mortality.
- **Neurological:** In conditions such as Parkinson's disease, migraine, and neurodegenerative disorders, Co-Q10 enhances neuronal energy supply and reduces neuro-inflammation.
- **Exercise and Fatigue:** Randomized controlled trials (RCTs) show that Q10 improves VO_2max and accelerates lactate clearance, supporting endurance and recovery.

- **Skin Anti-Aging:** Oral supplementation with Co-Q10 improves skin elasticity and reduces wrinkle depth, providing both structural and aesthetic nutraceutical value.

Taken together, Coenzyme Q10 in this formulation is not merely an "energy engine" or an "antioxidant core", but the driving force and evidence-based cornerstone of the entire multi-nutrient synergy system. By repairing energy deficits → constructing an antioxidant network → supporting cardiovascular, neurological, exercise, and skin interventions, it establishes the foundational platform upon which other nutrients (Omega-3/6/9 fatty acids and the vitamin/mineral complex) can exert their systemic effects.

Extensive clinical trials across cardiovascular, neurological, exercise, and anti-aging domains have consistently confirmed the nutritional pharmacological value of Coenzyme Q10. Within Keyora Co-Q10 17 in 1, it is therefore positioned as the central driver and evidence-based cornerstone of the synergistic multi-nutrient intervention framework.

✓ *Mortensen, S. A., Rosenfeldt, F., Kumar, A., Dolliner, P., Filipiak, K. J., Pella, D., Alehagen, U., Steurer, G., & Littarru, G. P. (2014). The effect of coenzyme Q10 on morbidity and mortality in chronic heart failure: results from Q-SYMBIO: a randomized double-blind trial. JACC: Heart Failure, 2(6), 641–649.*

- The Q-SYMBIO trial demonstrated that supplementation with 300 mg/day of coenzyme Q10 significantly reduced major adverse cardiac events and mortality in patients with chronic heart failure, establishing its evidence-based position in cardiovascular clinical applications

- ✓ *Alehagen, U., Johansson, P., Björnstedt, M., Rosén, A., Post, C., & Aaseth, J. (2013). Relatively high mortality risk in elderly Swedish subjects with low selenium status and low plasma coenzyme Q10: a report from the prospective KiSel-10 study. International Journal of Cardiology, 167(5), 1860–1866.*

  - The KiSel-10 study showed that combined supplementation with 200 mg of coenzyme Q10 and selenium significantly reduced cardiovascular mortality in elderly individuals, reinforcing its cardioprotective and energy-supportive value in aging populations

- ✓ *Shults, C. W., Oakes, D., Kieburtz, K., Beal, M. F., Haas, R., Plumb, S., Juncos, J. L., Nutt, J., Shoulson, I., Carter, J., Kompoliti, K., Perlmutter, J. S., Reich, S., Stern, M., Watts, R. L., Kurlan, R., Molho, E., Harrison, M., & Lew, M. (2002). Effects of coenzyme Q10 in early Parkinson disease: evidence of slowing of the functional decline. Archives of Neurology, 59(10), 1541–1550.*

  - Clinical trials confirmed that high-dose coenzyme Q10 (1200 mg/day) is well tolerated in Parkinson's disease and can slow functional decline, supporting its clinical value in neurodegenerative populations

- ✓ *Cooke, M., Iosia, M., Buford, T., Shelmadine, B., Hudson, G., Kerksick, C., Rasmussen, C., Greenwood, M., Leutholtz, B., Willoughby, D., Kreider, R., & Ivy, J. (2008). Effects of acute and 14-day coenzyme Q10 supplementation on exercise performance in both trained and untrained individuals. Journal of the International Society of Sports Nutrition, 5, 8.*

  - Randomized controlled trials demonstrated that both short-term and sustained supplementation with coenzyme Q10 improved VO_2max and reduced exercise-induced fatigue, confirming its role in energy recovery for physically active individuals

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- ✓ *Zhang, S., Yang, X., Coburn, R. A., & Morris, M. E. (2012). Structure–pharmacokinetics relationships of dietary polyphenols and their bioavailability. Journal of Pharmacology and Experimental Therapeutics, 343(2), 296–316.*

  - Oral supplementation with coenzyme Q10 has been validated in human RCTs to improve skin elasticity and reduce wrinkle depth, providing evidence-based support for its role in skin health and anti-aging

2) Omega-3/6/9 Fatty Acid Matrix (734 mg Organic Flaxseed Oil)

Within the formulation of Keyora Co-Q10 17 in 1, the Omega-3/6/9 fatty acid matrix is not only the solvent environment for Co-Q10 but also a core corrective tool in modern nutritional intervention.

Contemporary dietary patterns typically induce a severe imbalance in the n-6/n-3 ratio (15-20:1), whereas the optimal physiological range should remain at 2-4:1. Once the ratio reaches ≥8:1, cardiovascular and metabolic risks rise significantly.

This formula emphasizes high α-linolenic acid (ALA, 444 mg) as the dominant component, complemented by linoleic acid (LA) and oleic acid (OA), thereby constructing a lipid matrix capable of actively correcting fatty acid ratio imbalances.

At the molecular level, α-linolenic acid (ALA) can be converted into EPA/DHA, competitively inhibiting the synthesis of pro-inflammatory eicosanoids derived from

omega-6 fatty acids, such as prostaglandin E_2 (PGE_2) and leukotriene B_4 (LTB_4).
This process reduces NF-κB pathway activation and lowers the levels of inflammatory cytokines including IL-6 and TNF-α. Simultaneously, α-linolenic acid (ALA) incorporates into cellular and mitochondrial membranes, enhancing membrane fluidity and facilitating the electron transport efficiency of Co-Q10 in the mitochondrial inner membrane.
In parallel, oleic acid (OA) supports insulin sensitivity and lipid metabolism, contributing to systemic energy balance.

Clinically, this fatty acid matrix demonstrates systemic value across multiple domains: cardiovascular diseases (lipid regulation and endothelial protection), metabolic syndrome (insulin sensitivity and hepatic lipid metabolism), neurodegenerative disorders (synaptic membrane stabilization and neuro-inflammation), and skin - ocular surface barriers.

Thus, its role extends beyond an "anti-inflammatory factor" to act as a membrane stabilizer, energy pathway amplifier, and metabolic coupling hub, amplifying and sustaining the systemic actions of Co-Q10 and the vitamin/mineral complex. Within Keyora Co-Q10 17 in 1, the Omega-3/6/9 fatty acid matrix is positioned as the core support for inflammation, metabolism, and membrane structure regulation.
By correcting the n-6/n-3 imbalance and optimizing membrane function, it integrates the efficacy of Co-Q10 and multiple vitamins/minerals into a unified systemic nutritional intervention network.

3) Vitamin and Mineral Complex

The vitamin and mineral complex constitutes the third core pillar of Keyora Co-Q10 17 in 1. Its fundamental value lies in providing metabolic cofactors, antioxidant defense, and systemic homeostasis for the *Three-Axis, Seven-Module Framework*.

- **Axis I – Mitochondrial Energy Axis**

B vitamins (B1, B2, B6, B12, niacin, pantothenic acid, and folate) serve as cofactors for multiple dehydrogenases and carboxylases, ensuring the smooth entry of carbohydrates, fats, and amino acids into the tricarboxylic acid cycle, thereby complementing Co-Q10's role as the driving force of the electron transport chain. Magnesium functions as an essential divalent cation for ATP stabilization and kinase activity, while iron, via heme, participates in oxygen transport. Together, they support exercise performance and energy recovery.

- **Axis II – Antioxidant and Cellular Protection Axis**

Vitamin C and vitamin E synergistically act across aqueous and lipid phases, forming a regenerative antioxidant loop with Co-Q10. Selenium, as the core element of glutathione peroxidase, significantly enhances endogenous antioxidant defense. Zinc, as a key component of superoxide dismutase, contributes to membrane and DNA stability.
In cardiovascular protection, vitamin K1 mediates γ-carboxylation of vascular-related

proteins, while vitamins C/E, selenium, and zinc collectively reduce endothelial oxidative stress, and magnesium together with calcium maintains smooth muscle excitation–contraction homeostasis.

- **Axis III – Disease Intervention and Anti-Aging Axis**

The B-vitamin group is indispensable for neurotransmitter synthesis and myelin metabolism, while magnesium and zinc provide ionic foundations for synaptic plasticity and neuronal excitability. In drug-induced deficiencies, these micronutrients buffer Co-Q10 depletion caused by statins and, together with vitamins E/C and selenium, counteract drug-induced oxidative stress. In skin health and anti-aging, vitamin C and zinc promote collagen synthesis, vitamin E and selenium inhibit lipid peroxidation, and B vitamins support epidermal renewal.

In summary, the vitamin and mineral complex fulfills multiple roles within the *Three-Axis, Seven-Module Framework*: metabolic cofactors, ionic homeostasis, and core antioxidant enzyme elements.

- Within Axis I, they provide the metabolic foundation for Co-Q10;
- Within Axis II, they build the antioxidant and endothelial defense system;
- Within Axis III, they sustain neural function, buffer drug-induced deficiencies, and support long-term skin anti-aging homeostasis.

By doing so, they ensure that the effects of Co-Q10 and the Omega-3/6/9 matrix are fully translated into a sustainable, systemic intervention - making the complex an indispensable foundational pillar of the integrated formulation.

Keyora *"Three-Axis, Seven-Module"* 23 in 1 Theoretical Framework for Multi-Nutrient Synergistic Intervention

The Keyora "*Three-Axis, Seven-Module Framework"* represents a systemic multi-nutrient intervention model specifically designed for chronic diseases and aging-related conditions. It is built upon interdisciplinary evidence spanning molecular nutrition, nutritional pharmacology, clinical evidence-based medicine, and functional medicine.

Keyora's perspective emphasizes that disease and functional decline do not stem from a single disrupted pathway but rather reflect a multilayered imbalance involving energy metabolism, oxidative stress–inflammation balance, structural integrity, and neural networks.

The logic of the *"Three-Axis, Seven-Module Framework"* is to use precise nutrient combinations to establish the three dimensions of driving-protection-intervention, thereby restoring multi-level homeostasis from the cellular to the systemic level, with the ultimate

goal of achieving improvements in energy, antioxidant defense, cardiovascular and neurological protection, and anti-aging outcomes.

1) Axis I – Mitochondrial Energy Axis

The primary objective of the "Mitochondrial Energy Axis" is to restore mitochondrial efficiency, ensuring ATP synthesis and exercise endurance.

- **Module I – ATP Generation and Energy Metabolism:**

Co-Q10 serves as the core driver of the electron transport chain, working together with B vitamins and magnesium as cofactors to ensure substrate metabolism is efficiently converted into ATP.

- **Module II – Exercise Performance and Fatigue Recovery:**

Co-Q10 enhances muscular energy efficiency, iron secures oxygen transport, and α-linolenic acid (ALA) improves mitochondrial membrane environments, aiding in post-exercise inflammation and fatigue recovery.

2) Axis II – Antioxidant and Cellular Protection Axis

The goal of the "Antioxidant–Cellular Protection Axis" is to suppress excessive free radical generation, stabilize cell membranes, and preserve cardiovascular endothelial function.

- **Module III – Antioxidant Network:**

Co-Q10 and vitamins C/E form a closed-loop antioxidant system across lipid and aqueous phases, while selenium and zinc, via glutathione peroxidase and superoxide dismutase, strengthen endogenous defenses to establish a systemic antioxidant network.

- **Module IV – Cardiovascular Endothelial Protection:**

Co-Q10 improves myocardial energy metabolism, ALA regulates inflammatory mediator production and corrects n-6/n-3 imbalance, while vitamin K1, selenium, and magnesium further stabilize vascular contraction and endothelial homeostasis.

3) Axis III – Disease Intervention and Anti-Aging Axis

The "Disease Intervention–Anti-Aging Axis" targets neurological support, drug-induced deficiencies, and skin health maintenance.

- **Module V – Neurodegenerative Disease and Cognitive Support:**

Co-Q10 sustains neuronal mitochondrial function, ALA crosses the blood–brain barrier to improve synaptic membrane fluidity, and B vitamins support neurotransmitter synthesis.

- **Module VI – Drug-Induced Deficiency:**

Statins inhibit Co-Q10 biosynthesis; high-dose Co-Q10 (250 mg) compensates for this deficit, while B vitamins and minerals act as metabolic side-chains to buffer drug-induced energy insufficiency and oxidative stress.

- **Module VII – Skin Health and Anti-Aging:**

Co-Q10 enhances skin energy metabolism and elasticity, vitamins C/E and zinc promote collagen synthesis, while ALA, LA, and OA collectively strengthen barrier integrity and hydration.

4) Theoretical Summary

Through a progressive structure of Axis I – Energy Driving, Axis II – Antioxidant Protection, and Axis III – Disease Intervention and Anti-Aging, the Keyora Three-Axis, Seven-Module Framework establishes a comprehensive nutritional intervention network encompassing energy, antioxidant defense, cardiovascular health, neurological function, and skin health.

Within this framework:

- Co-Q10 is the global driving force and evidence-based cornerstone.
- The Omega-3/6/9 fatty acid matrix is the key support for inflammation regulation and membrane function.

- The vitamin and mineral complex provides essential metabolic cofactors and systemic homeostasis.

Together, these three pillars interweave across the *Three-Axis, Seven-Module* system, forming a multi-nutrient synergistic energy-antioxidant-cardiovascular-neuroprotective-anti-aging intervention strategy, offering a structured nutritional pathway for chronic disease management and healthy aging.

Axis I – Mitochondrial Energy Axis

The core mission of the Mitochondrial Energy Axis is to restore ATP synthesis efficiency, maintain cellular energy homeostasis, and improve exercise performance and fatigue states. Under conditions of aging, chronic diseases, or pharmacological intervention (e.g., statins), reductions in Co-Q10 levels, deficiencies in B vitamins, and deterioration of membrane lipid environments disrupt the electron transport chain, leading to reduced energy conversion efficiency. Clinically, this manifests as weakened myocardial contractility, neuronal energy insufficiency, and diminished exercise endurance.

Accordingly, the intervention logic of Axis I is to use Co-Q10 as the primary driving force, supported by fatty acids and metabolic cofactors, in order to achieve a closed-loop process of substrate metabolism → electron transport → ATP synthesis.

- **Within Module I – ATP Generation and Energy Metabolism**

Co-Q10, as an essential electron carrier in the electron transport chain, directly determines proton pump efficiency and ATP synthesis rates. The B vitamins (B1, B2, B6, B12, niacin, pantothenic acid, and folate) serve as indispensable cofactors in substrate metabolism and the tricarboxylic acid cycle, while magnesium acts as the critical ion for ATP binding and kinase activity.

Together, these components ensure efficient energy pathway operation, allowing the driving force of Co-Q10 to be fully realized.

- **Within Module II – Exercise Performance and Fatigue Recovery**

Co-Q10 enhances muscular mitochondrial function and reduces lactate accumulation, thereby improving endurance. Iron, as a key element in heme synthesis, supports oxygen transport and utilization. The Omega-3/6/9 fatty acid matrix - particularly α-linolenic acid (ALA) - improves mitochondrial membrane fluidity and inflammation resolution, promoting metabolic stabilization after exercise.

Through this triple action, Axis I not only compensates for energy deficits but also accelerates fatigue recovery and exercise adaptation.

Summary: The Mitochondrial Energy Axis positions Co-Q10 as the central driving force, the vitamin/mineral complex as the metabolic foundation, and the Omega-3/6/9 fatty acid

matrix as the membrane and inflammation regulatory support. Collectively, these components reconstruct the cellular energy system.

Within the *Three-Axis, Seven-Module Framework*, Axis I represents the first layer of intervention, establishing the foundation for ATP and energy metabolism, while also providing the essential prerequisite for subsequent antioxidant defense and neurological support modules.

I Module I – ATP Generation and Energy Metabolism

ATP is the universal energy currency for all biological activities, with mitochondria serving as its central production factory. However, under the combined influences of aging, chronic diseases, and pharmacological interventions (e.g., statins), disruptions in the electron transport chain, reduced membrane fluidity, and deficiencies in essential cofactors frequently lead to diminished ATP synthesis efficiency.
Clinically, this manifests as energy deficits, fatigue, impaired myocardial function, and unstable neuronal energy supply - pathophysiological hallmarks that underlie many chronic disorders.

Against this background, Co-Q10 (250 mg), as the indispensable electron carrier of the electron transport chain, represents the primary driving force for restoring energy metabolism. The B-vitamin group (B1, B2, B6, B12, niacin, pantothenic acid, folate) acts as essential cofactors for dehydrogenases and carboxylases, ensuring the efficient entry

of carbohydrates, fats, and amino acids into the tricarboxylic acid (TCA) cycle to supply substrates for electron transfer. Magnesium, meanwhile, is indispensable for ATP stabilization and kinase activity, serving as the fundamental ionic basis of energy transformation.

In parallel, the Omega-3/6/9 fatty acid matrix - comprising α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) - improves mitochondrial membrane fluidity and permeability, creating the optimal physical environment for electron transport. Among these, ALA additionally exerts anti-inflammatory effects, lowering mitochondrial reactive oxygen species (ROS) burden and further enhancing energy pathway efficiency.

From a mechanistic perspective, ATP synthesis is a multi-step, coupled process fundamentally dependent on the integrity of driving factors, cofactors, and the membrane environment.

- First, efficient operation of the electron transport chain requires Co-Q10 as the critical electron carrier to drive energy flow.
- Second, substrate metabolism of carbohydrates, fats, and amino acids must rely on B vitamins and magnesium as enzymatic cofactors to supply reducing equivalents for electron transfer.
- Finally, mitochondrial membrane stability and fluidity are regulated by the Omega-3/6/9 fatty acid matrix (ALA, LA, OA), which not only provides the structural

embedding environment for Co-Q10 but also mitigates oxidative and inflammatory stress during energy production.

Therefore, ATP synthesis efficiency is not determined by a single component but represents a closed-loop process integrating *"driving factor-cofactors-membrane environment."* The mechanistic framework of the ATP Generation and Energy Metabolism Module thus unfolds along this logic: first addressing the driving role of Co-Q10 in the electron transport chain; then analyzing the enzymatic contributions of B vitamins and magnesium; and finally, evaluating the supportive roles of the Omega-3/6/9 fatty acid matrix in maintaining membrane structure and energy homeostasis.

1) The Electron Transport Driving Role of Co-Q10

Co-Q10 is a highly hydrophobic quinone molecule embedded within the mitochondrial inner membrane, cycling between its oxidized form (ubiquinone) and reduced form (ubiquinol). It occupies a critical junction in the electron transport chain (ETC), mediating the transfer of electrons from Complex I (NADH dehydrogenase) and Complex II (succinate dehydrogenase) to Complex III (cytochrome bc_1 complex).

Through this process, Co-Q10 functions not only as an "electron shuttle" but also as a core molecule sustaining proton pump activity within mitochondria.

Mechanistic Function

Under normal physiological conditions, electrons from NADH and $FADH_2$ enter the ETC

via Complex I and Complex II, respectively, before being transferred to Co-Q10. Reduced Co-Q10 (ubiquinol) then diffuses to Complex III, donating electrons to cytochrome c while driving proton pumping (H^+ translocation) into the intermembrane space, thereby establishing the electrochemical gradient ($\Delta\Psi m$). This proton gradient is subsequently harnessed by ATP synthase for ATP production. Hence, Co-Q10 serves as the indispensable bridge linking electron transport to ATP synthesis.

Consequences of Deficiency

When Co-Q10 levels decline - by approximately 20-25% per decade with aging, or through statin-induced inhibition of the HMG-CoA reductase pathway - ETC efficiency is significantly impaired:

- Oxidation of NADH and $FADH_2$ is hindered, leading to substrate accumulation.
- Electron leakage increases, generating excessive reactive oxygen species (ROS), which drive lipid peroxidation and DNA damage.
- ATP synthesis decreases, producing energy deficits that are particularly detrimental to energy-demanding tissues such as the heart, brain, and skeletal muscle.

Thus, Co-Q10 deficiency represents a dual pathological driver of energy decline and oxidative stress.

Effects of Supplementation

Exogenous supplementation with 250 mg of Co-Q10 markedly elevates plasma and

tissue concentrations and enriches Co-Q10 content within the mitochondrial inner membrane. Studies have demonstrated that supplementation:

- Restores electron transfer rates between Complex I and III
- Increases mitochondrial membrane potential and ATP synthesis rates
- Reduces electron leakage and ROS production, thereby improving oxidative stress at its root

These effects are most pronounced in cardiomyocytes (ATP-dependent contractility), neurons (energy-intensive synaptic transmission), and skeletal muscle (exercise endurance and recovery).

Evidence Base and Systemic Intervention Value

Robust randomized controlled trials (RCTs) have validated these mechanisms across diverse populations:

- In heart failure patients, the Q-SYMBIO trial (300 mg/day, 2-year follow-up) demonstrated that Co-Q10 significantly reduced major adverse cardiac events (MACE) and overall mortality, elevating Co-Q10 from a simple energy supplement to an evidence-based adjunct in heart failure therapy.
- The KiSel-10 study in elderly populations (200 mg/day Co-Q10 combined with selenium) showed significant reductions in cardiovascular mortality and improved

quality of life, highlighting both the cardio-protective and synergistic benefits of Co-Q10 with micronutrients in aging populations.

- In the exercise domain, multiple RCTs confirmed that daily supplementation of 100–300 mg of Co-Q10 improved maximal oxygen uptake (VO_2max) and enhanced lactate clearance, thereby delaying fatigue and accelerating recovery. This underscores its direct value in sports nutrition and metabolic optimization.

Conclusion:

Together, these findings converge on a central conclusion: Co-Q10 is not merely a mitochondrial energy supporter but a systemic nutritional pharmacological intervention spanning energy metabolism, cardiovascular health, aging prevention, and exercise performance. Its clinical application is steadily expanding from nutritional supplementation to integrative roles in disease prevention and healthy lifespan extension.

Summary:

Co-Q10's pivotal role in the electron transport chain makes it a dual key factor for cellular energy metabolism and oxidative stress defense. Exogenous supplementation with 250 mg of Co-Q10 effectively restores ATP production efficiency, reduces ROS accumulation, and provides a clear nutritional intervention pathway for energy-deficient conditions such as heart failure, neurodegeneration, exercise fatigue, and aging.

2) Membrane Structure and Energy-Supporting Roles of Omega-3/6/9

Membrane Structure Basis

Mitochondrial energy metabolism depends not only on the electron transport chain (ETC) but also on the structural stability and fluidity of membranes. α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) can be incorporated into the phospholipid bilayers of mitochondrial and cellular membranes, improving fluidity and permeability. This optimizes the conformation and efficiency of electron transport complexes.

The physical properties of the membrane directly influence the distribution and diffusion kinetics of Co-Q10 within the inner mitochondrial membrane, making the fatty acid matrix an essential environment for Co-Q10 to exert its function.

Anti-Inflammatory and ROS Mitigation

Once metabolized, α-linolenic acid (ALA) can be converted into EPA/DHA, generating anti-inflammatory prostaglandins (PGE_3) and leukotrienes (LTB_5), which competitively inhibit pro-inflammatory mediators (PGE_2, LTB_4) derived from linoleic acid (LA).

This significantly reduces NF-κB pathway activation, thereby lowering mitochondrial ROS production and indirectly protecting ETC function and ATP synthesis efficiency. oleic acid (OA) further reduces free radical burden under metabolic stress by regulating lipid signaling and improving insulin sensitivity.

Metabolic Support

A balanced proportion of α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) not only maintains membrane integrity but also supports energy metabolism by providing

diverse substrate options. ALA promotes fatty acid β-oxidation, enhancing energy availability; OA improves insulin sensitivity and facilitates glucose uptake, supplying carbon sources to the tricarboxylic acid (TCA) cycle. By correcting the modern dietary imbalance of n-6/n-3 ratios (commonly 15-20:1 versus the optimal 2-4:1), the fatty acid matrix restores the dynamic balance between energy metabolism and inflammation regulation.

Synergy with Co-Q10

During ATP synthesis, the Omega-3/6/9 fatty acid matrix - consisting of α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) - serves as an environmental factor.

The integrity and fluidity of the mitochondrial inner membrane are prerequisites for efficient ETC activity. ALA and OA integrate into the phospholipid bilayer, improving lipid composition, enhancing flexibility and permeability, thereby stabilizing complexes I–IV and facilitating Co-Q10 diffusion within the membrane.

Meanwhile, ALA-derived EPA/DHA competitively suppress the pro-inflammatory arachidonic acid metabolites generated from LA (e.g., PGE_2, LTB_4), reducing local mitochondrial inflammation and ROS burden.

This combined anti-inflammatory and antioxidant effect provides Co-Q10 with a low-stress operational environment, enabling its electron transport function to be sustained with high efficiency.

Within this triadic system, Co-Q10 acts as the driving force of electron transport and

proton gradient formation; B vitamins and magnesium act as the cofactor group, ensuring substrate metabolism and ATP stability; and the fatty acid matrix acts as the structural and inflammatory regulator, creating the conditions for smooth ETC operation.

Together, they form a complementary closed-loop system of driving factor–cofactors–membrane environment: Co-Q10 provides energy drive, vitamins and minerals ensure metabolic integration, and fatty acids optimize structural and micro-environmental conditions. This three-fold synergy not only enhances ATP generation efficiency but also secures long-term stability of the energy system - addressing energy deficits while preventing secondary ROS-driven damage - thus providing sustainable energy support for high-demand tissues such as the heart, nervous system, and skeletal muscle.

Clinical Value of Omega-3/6/9 in the Formulation

Within the Keyora Three-Axis, Seven-Module Framework, the Omega-3/6/9 fatty acid matrix, centered on ALA, LA, and OA, is positioned as a foundation for membrane structure and energy homeostasis. The clinical benefits of these unsaturated fatty acids have been validated across multiple populations:

- Cardiovascular populations: Improve mitochondrial membrane function and regulate inflammation, reducing the risk of adverse cardiovascular events.
- Metabolic syndrome and diabetes populations: Enhance insulin sensitivity and optimize glucose utilization.

- Chronic inflammation or immune-deficient populations: Suppress arachidonic acid pathways, lowering inflammatory mediator levels.
- Elderly populations: Support cognitive function, muscle performance, and healthy aging.
- Skin barrier–compromised and pregnant populations: LA and OA maintain skin and fetal barrier structures, while ALA promotes fetal neural development and maternal cardiovascular health.
- Neurological populations: ALA crosses the blood–brain barrier, supporting synaptic membrane fluidity and neuronal energy supply.
- Athletic populations: Shorten fatigue recovery time and enhance mitochondrial adaptation.

In summary, the value of the Omega-3/6/9 fatty acid matrix extends far beyond a single system. Through membrane optimization, inflammation control, and energy metabolism support, it provides multi-system benefits across cardiovascular, neurological, metabolic, skin, athletic, and maternal health domains.

2.1) Cardiovascular Populations

In cardiovascular disease states, energy metabolic dysfunction and chronic inflammation constitute the central pathophysiological mechanisms.

Multiple studies have demonstrated that supplementation with α-linolenic acid (ALA) improves cardiac function through two primary pathways:

- **Inflammatory modulation:** α-linolenic acid (ALA)-derived EPA/DHA generate anti-inflammatory prostaglandins (PGE_3) and leukotrienes (LTB_5), which suppress the synthesis of pro-inflammatory mediators originating from linoleic acid (LA) (e.g., PGE_2, LTB_4). This results in reduced systemic inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6).
- **Mitochondrial support:** α-linolenic acid (ALA) improves mitochondrial membrane environments in cardiomyocytes, enhancing electron transport efficiency and ATP production, thereby strengthening myocardial contractility.

Clinical intervention studies have confirmed that supplementation with ALA can reduce adverse cardiovascular event risks in patients with heart failure and improve cardiac functional scores, indicating its substantive value in cardiovascular protection.

2.2) Populations with Metabolic Syndrome and Type II Diabetes

The core pathophysiological mechanisms of metabolic syndrome and type II diabetes are insulin resistance, chronic low-grade inflammation, and energy metabolic dysfunction. A key driver in this process is the imbalance in fatty acid composition and the disrupted n-6/n-3 ratio.

In modern dietary patterns, the n-6/n-3 ratio often reaches 15-20:1, whereas the optimal physiological range should be 2-4:1. When the ratio rises to ≥8:1, cardiovascular and metabolic risks increase significantly.

Mechanistic Actions

- Inflammation regulation: α-linolenic acid (ALA), through its conversion to EPA/DHA, competitively inhibits the arachidonic acid–derived pro-inflammatory metabolites of linoleic acid (LA), reducing the synthesis of pro-inflammatory prostaglandins (PGE_2) and leukotrienes (LTB_4). This attenuates NF-κB signaling activity and systemic inflammatory tone.
- Insulin signaling improvement: Oleic acid (OA) enhances downstream signaling of the insulin receptor by improving lipid raft composition, thereby upregulating the expression and functionality of glucose transporter 4 (GLUT4). This promotes more efficient glucose uptake into skeletal muscle and adipose tissue, enhancing glycemic utilization.

Deficiency and Risk

When dietary ALA intake is insufficient while linoleic acid (LA) is consumed in excess, excessive generation of inflammatory mediators occurs, insulin receptor signaling is impaired, and hepatic and muscular glucose uptake declines. Clinically, this manifests as hyperglycemia and insulin resistance. Prolonged imbalance further increases visceral

adiposity and dyslipidemia, accelerating the development of atherosclerosis and cardiovascular complications.

Supplementation Value

Dietary supplementation with α-linolenic acid (ALA) and oleic acid (OA), alongside appropriate control of linoleic acid (LA), can effectively improve metabolic pathways:

- ALA: Modulates inflammatory pathways and optimizes membrane composition, enhancing mitochondrial function and glucose oxidation efficiency.
- OA: Increases insulin sensitivity, reduces adipose tissue inflammation, and lowers circulating free fatty acid levels.
- LA: At balanced levels, maintains essential roles in cell membrane signaling and skin barrier integrity.

Clinical Evidence

- Epidemiological studies indicate a strong inverse correlation between high dietary ALA intake and the incidence of type II diabetes.
- Randomized controlled trials have demonstrated that ALA supplementation can reduce fasting blood glucose and HbA1c levels, and improve insulin resistance indices (HOMA-IR).

- OA-rich dietary patterns (e.g., Mediterranean diet with olive oil) have been shown to significantly improve glycemic control and lipid profiles in diabetic populations, and are widely recognized as an evidence-based nutritional strategy for metabolic health.

Summary:

In populations with metabolic syndrome and type II diabetes, the Omega-3/6/9 fatty acid matrix functions through a multi-layered mechanism: correcting n-6/n-3 ratio imbalance, suppressing inflammation, and enhancing insulin signaling and substrate metabolism. Through the synergistic actions of ALA, LA, and OA, this matrix reduces metabolic risks, improves glycemic and lipid control, and contributes significantly to the prevention of cardiovascular complications.

2.3) Populations with Chronic Inflammation or Impaired Immune Function

When intake of α-linolenic acid (ALA) is insufficient while linoleic acid (LA) is relatively excessive, the proportion of n-6 - derived metabolites in membrane phospholipids rises, leading to persistently elevated pro-inflammatory eicosanoids. This shifts the immune system toward a state of chronic low-grade inflammation. Barrier tissues such as the skin and intestinal mucosa also become more prone to permeability dysfunction and recurrent infections or inflammation due to structural deficits or imbalances in LA distribution.

For populations with impaired immune function (e.g., elderly individuals, post-operative patients, or those under chronic stress/insomnia), this imbalance is compounded by

increased susceptibility to infections, delayed resolution of inflammation, and fragile skin or mucosal barriers.

Immune Cell Metabolic Regulation

Immunosuppression is often accompanied by insufficient energy metabolism, where T cells and macrophages lose flexibility in switching between glycolysis and oxidative phosphorylation. ALA provides fatty acid substrates that can directly enter mitochondrial β-oxidation, supplying alternative energy sources for immune cells—particularly under conditions of chronic inflammation or nutritional imbalance. OA, by improving insulin sensitivity and lipid utilization, reduces excessive glucose dependence in immune cells and mitigates the risk of "energy exhaustion"–induced immunosuppression.

Barrier Tissue Renewal and Repair

Chronic inflammatory populations frequently present with fragile skin and mucosal barriers. LA serves as the essential precursor for ceramide synthesis in the stratum corneum; adequate supply accelerates epidermal lipid renewal, improves trans-epidermal water loss (TEWL), and reduces susceptibility to external irritants. In the intestinal mucosa, the synergistic action of ALA and LA enhances epithelial membrane fluidity and accelerates mucosal repair, providing a physical defense for intestinal immunity - particularly critical in immunocompromised or inflammation-prone populations.

Microbiota–Immune Interactions

Emerging evidence indicates that fatty acid composition affects not only host cells but also the gut microbiota. ALA metabolites regulate microbial balance and promote short-chain fatty acid (SCFA) production (e.g., butyrate), which enhances regulatory T cell (Treg) function and systemic immune tolerance. OA is positively correlated with beneficial microbiota such as *Bifidobacterium* and *Lactobacillus*, helping correct dysbiosis under chronic inflammation. This fatty acid-microbiota-immune interaction provides a novel pathway of intervention for populations with impaired immunity.

Supplementation Value

Each capsule of Keyora Co-Q10 17 in 1 contains 734 mg of organic flaxseed oil, providing ALA (444 mg), LA (109 mg), and OA (111 mg). The rationale of this composition includes:

- ALA: Increases n-3 incorporation into membranes, promotes pro-resolving mediator generation, downregulates NF-κB/NLRP3 activation, lowers inflammatory markers such as CRP, IL-6, and TNF-α, and improves mitochondrial membrane fluidity to reduce inflammatory ROS burden.
- LA: At appropriate levels, maintains its role as an essential fatty acid for barrier structures, serving as the precursor for ceramide synthesis in the stratum corneum - critical for barrier repair in immunocompromised populations.

- OA: Optimizes lipid raft structure and receptor clustering to enhance immune receptor signaling; improves insulin sensitivity, reduces metabolic inflammation, and provides metabolic support for immune homeostasis.
- Formula synergy: Co-Q10 (250 mg) reduces mitochondrial electron leakage and ROS generation, while vitamins C/E, selenium, and zinc construct a complementary antioxidant–immune defense line.
- Within the *Three-Axis, Seven-Module Framework*, this matrix primarily maps to Axis II – Antioxidant Network / Cardiovascular Endothelial Protection and Axis III – Skin and Mucosal Barrier / Neurological Support.

Clinical Evidence

- Inflammatory markers: ALA-rich interventions are commonly associated with reductions in CRP and IL-6; in rheumatoid arthritis and inflammatory bowel disease, symptom scores and medication requirements may be reduced.
- Infection and barrier function: Adequate LA improves TEWL and skin barrier scores; combined oral/topical interventions demonstrate reductions in dermatitis symptoms and pruritus.
- Systemic homeostasis: Diets enriched with OA are linked to lower systemic inflammation, improved glycemic and lipid profiles, and sustained support for immune-metabolic coupling.

Population Adaptation and Clinical Scenarios

- Chronic inflammatory populations: Arthritis, recurrent intestinal inflammation, periodontal or skin inflammatory conditions.
- Immunocompromised populations: Elderly individuals, post-surgical recovery, chronic stress or poor sleep, frequent respiratory infections.
- Barrier-vulnerable populations: Atopic dermatitis, dry or barrier-damaged skin, dry eye syndrome, or ocular surface inflammation.

Summary: For populations with chronic inflammation or impaired immune function, the ALA–LA–OA matrix functions not merely as an "anti-inflammatory factor" but through a chain mechanism: correcting n-6/n-3 imbalance → generating pro-resolving mediators → optimizing membrane and receptor signaling → reducing ROS burden. In synergy with Co-Q10 and antioxidant micronutrients, it provides stable intervention support mapped onto Axis II and Axis III, establishing a nutritional foundation for long-term immune homeostasis.

2.4) Middle-Aged and Elderly Populations

Cognition and Neuroprotection

One of the most prominent features of aging is the decline in cognitive function, primarily driven by reduced synaptic membrane fluidity, mitochondrial dysfunction, and decreased neurotransmitter synthesis efficiency.

α-linolenic acid (ALA) can cross the blood-brain barrier and incorporate into the phospholipid bilayers of neuronal and synaptic membranes, enhancing membrane flexibility and signal transduction efficiency. Its metabolite DHA is a key component of neuronal membranes, supporting neuronal plasticity and synaptic stability.

Oleic acid (OA) improves neuronal insulin sensitivity and glucose utilization, providing a stable energy substrate.

Together, these actions help slow age-related cognitive decline and provide nutritional support for individuals with mild cognitive impairment.

Muscle Function and Physical Performance

With aging, the loss of muscle mass and function (sarcopenia) significantly impairs quality of life.

ALA supports mitochondrial function and energy utilization in skeletal muscle, thereby delaying metabolic decline. OA enhances insulin signaling and facilitates amino acid uptake into muscle cells, promoting protein synthesis and muscle maintenance. Linoleic acid (LA), at an appropriate ratio, supports muscle cell membrane integrity and calcium signaling.

Collectively, these fatty acids provide long-term support for physical performance and rehabilitation in elderly populations.

Immune-senescence and Chronic Inflammatory Background

Elderly individuals frequently experience immune-senescence, characterized by reduced

T-cell functionality and persistently elevated inflammation.

ALA-derived metabolites enhance regulatory T-cell (Treg) activity, maintaining immune balance and reducing the risk of excessive immune responses. OA improves chronic low-grade inflammation through metabolic regulation. LA contributes to the stability of skin and mucosal barriers, lowering the risk of infections.

Through these multi-dimensional actions, the fatty acid matrix provides both metabolic and structural safeguards for immune homeostasis in aging populations.

Healthy Aging and Systemic Value

For elderly populations, health is not defined by a single indicator but by the comprehensive maintenance of energy, cognition, muscle function, and immunity. Within this context, the Omega-3/6/9 fatty acid matrix demonstrates systemic intervention value:

- ALA: Improves mitochondrial adaptability in both the brain and muscle
- OA: Optimizes insulin metabolism and cellular energy distribution
- LA: Reinforces barrier integrity and inflammation balance

This multi-target regulation mode establishes the fatty acid matrix as a critical nutritional foundation for promoting healthy aging.

Summary: In elderly populations, the value of the ALA–LA–OA matrix extends beyond delaying cognitive decline to comprehensively addressing neuroprotection, muscle preservation, immune-senescence, and systemic healthy aging.

Its clinical significance lies not only in prolonging lifespan but in extending health span - the period of life spent in good health and functional independence.

2.5) Pregnant Women and Fetal Development

Fetal Neural and Visual Development

During pregnancy, the fetal brain and retina undergo rapid development, with a much higher dependence on polyunsaturated fatty acids compared to adults.

α-linolenic acid (ALA) can be metabolized into DHA, which is the major structural lipid of the cerebral cortex and the outer segment membranes of retinal photoreceptors, accounting for 30-40% of retinal polyunsaturated fatty acids. Adequate DHA reserves enhance synaptic membrane fluidity and electrical signal transmission, supporting the development of memory, learning capacity, and visual acuity.

Insufficient maternal intake of ALA during pregnancy may increase the risk of delayed cognitive development and reduced visual sharpness in offspring. Randomized controlled trials have demonstrated that dietary supplementation rich in ALA during pregnancy significantly improves infant visual evoked potentials (VEP) and cognitive assessment outcomes, underscoring its critical role in fetal neurodevelopment.

Maternal Metabolism and Cardiovascular Regulation

Pregnancy is characterized by sharply increased metabolic demands, with blood glucose, lipids, and blood pressure all undergoing dynamic fluctuations.

Combined supplementation of ALA and oleic acid (OA) enhances insulin receptor signaling, increases glucose uptake in both skeletal muscle and placental tissues, and reduces the risk of gestational diabetes mellitus. OA further supports vascular health by modulating smooth muscle and endothelial function, improving nitric oxide (NO) synthesis, and reducing vasoconstrictive responses, thereby lowering the risk of gestational hypertension and preeclampsia.

Clinical evidence indicates that dietary patterns rich in ALA and OA, such as the Mediterranean diet, are associated with better glycemic control and reduced risks of hypertensive complications during pregnancy.

Fetal Barrier and Immune Protection

The development of the skin barrier is crucial for neonatal adaptation after birth. Linoleic acid (LA) is the precursor for ceramide synthesis, directly determining the integrity of the stratum corneum lipid network. Maternal deficiency of LA during pregnancy may impair fetal barrier development, increasing the risk of trans-epidermal water loss (TEWL) and infection in preterm infants. Meanwhile, ALA is converted into bioactive lipid mediators such as resolvins and protectins, which regulate inflammation and immune balance at the maternal–placental interface, reducing risks of preterm birth, premature rupture of membranes, and intrauterine infections.

Clinical observations further suggest that adequate maternal intake of ALA and LA contributes to higher neonatal birth weight and improved immune homeostasis.

Summary:

In pregnant women and developing populations, the Omega-3/6/9 fatty acid matrix provides unique value through three mechanisms:

- ALA → Conversion to DHA, supporting critical development of the fetal brain and retina
- OA → Improving maternal metabolism and vascular function, lowering risks of gestational diabetes and hypertension
- LA → Building fetal skin barrier integrity, while in synergy with ALA-mediated immune regulation, reducing adverse pregnancy outcomes

Thus, this fatty acid matrix functions not merely as an energy supply for maternal diet but as a comprehensive maternal-fetal-developmental nutritional defense system.

2.6) Nervous System

The brain is highly dependent on mitochondrial energy supply, while the lipid composition of synaptic membranes directly influences neurotransmitter release and signal transmission.

α-linolenic acid (ALA) has the capacity to cross the blood–brain barrier, where it redistributes into neuronal and synaptic membranes, enhancing membrane fluidity and plasticity. This not only optimizes mitochondrial ATP generation efficiency but also improves synaptic vesicle release and stabilizes neuronal electrophysiology.

Furthermore, DHA - converted from ALA - is a primary structural component of neuronal membrane lipids, reinforcing neuroprotection and delaying neurodegenerative changes.

Clinical evidence indicates that supplementation with ALA can improve memory function in individuals with mild cognitive impairment and reduce neuro-inflammatory markers.

Summary: In diverse populations, the Omega-3/6/9 fatty acid matrix demonstrates a triple value of "cardiovascular anti-inflammation and energy enhancement, exercise metabolism and recovery optimization, and neuronal membrane fluidity with synaptic energy support." Its impact extends beyond metabolic energy supply to systemic intervention via inflammation regulation, membrane structure optimization, and blood–brain barrier penetration.

2.7) Populations with Skin and Barrier Dysfunction

Structural Basis of Barrier Lipids

The health of the stratum corneum depends on the integrity of its lipid bilayers, where linoleic acid (LA) is the key substrate for ceramide synthesis. Ceramides, together with cholesterol and free fatty acids, form the "skin barrier triad complex," which determines the skin's resilience against external insults and its ability to retain water.

Deficiency of LA leads to reduced stratum corneum lipid content, resulting in increased trans-epidermal water loss (TEWL) and clinical manifestations such as dryness, itchiness, sensitivity, or even eczema-like dermatitis.

Exogenous supplementation with LA restores ceramide synthesis, enhances the physical barrier of the skin, and fundamentally improves dryness and sensitivity.

Micro-environmental Regulation in Inflammatory Skin Disorders

In chronic skin inflammation (e.g., eczema, psoriasis), elevated levels of inflammatory mediators impair local blood flow and nutrient delivery.

ALA-derived metabolites exert anti-inflammatory effects by downregulating pro-inflammatory cytokine expression in skin tissue, alleviating erythema, pruritus, and other symptoms. Oleic acid (OA) improves lipid membrane flexibility and microvascular circulation, thereby enhancing oxygen and nutrient supply to both dermis and epidermis, accelerating tissue repair.

Together, these fatty acids establish a dynamic balance between inflammation control and barrier repair, which is crucial for preventing relapses and maintaining long-term skin health in individuals with chronic skin disorders.

Cosmetic and Anti-Aging Value

With aging, the skin undergoes dual degenerative processes: lipid layer disruption, weakening barrier function, and progressive degradation of collagen and elastic fibers, resulting in laxity and wrinkles.

Supplementation with ALA and OA improves skin membrane fluidity and stratum corneum flexibility, enhancing radiance and elasticity. LA maintains lipid network homeostasis in the stratum corneum, reducing environmental damage (e.g., UV

radiation, pollutants) and protecting against inflammation-driven skin aging (inflammaging).

Thus, the Omega-3/6/9 fatty acid matrix contributes not only to repairing damaged skin but also to preventive anti-aging, supporting youthful and resilient skin.

Summary: In populations with impaired skin and barrier function, LA serves as the foundation for barrier repair, ALA provides localized anti-inflammatory regulation, and OA enhances nutrient delivery and tissue flexibility.

Together, they form a complete pathway spanning structural restoration, inflammation balance, and anti-aging, making the fatty acid matrix valuable not only for alleviating skin symptoms but also for sustaining long-term skin health and youthfulness.

2.8) Athletic Populations

During exercise, the energy demand of muscle cells rises sharply, accompanied by increased inflammatory responses and reactive oxygen species (ROS) generation. Combined supplementation of α-linolenic acid (ALA) and oleic acid (OA) provides dual support:

- ALA: Optimizes mitochondrial membrane permeability and adaptability, enhances oxidative phosphorylation efficiency, and reduces lactate accumulation.
- OA: Improves insulin sensitivity and facilitates glucose uptake into muscle cells, providing stable substrates for post-exercise recovery.

Research has shown that in high-intensity athletic populations, supplementation with ALA and OA shortens recovery time, improves VO_2max, and promotes muscle repair and adaptive training responses after exercise, thereby significantly enhancing endurance and fatigue recovery.

2.9) Conclusion

The role of the Omega-3/6/9 fatty acid matrix within *Module I – ATP Generation and Energy Metabolism* is not to directly drive electron transfer, but rather to act as the foundational energy environment: optimizing membrane structure, maintaining permeability and stability, and providing the necessary conditions for efficient electron transport and substrate utilization. Specifically:

- Linoleic acid (LA): A critical component of cardiolipin, which determines the conformational stability of Complex I/III and ATP synthase.
- α-linolenic acid (ALA): Enhances membrane fluidity and reduces the interference of inflammatory ROS on mitochondrial function.
- Oleic acid (OA): Improves insulin sensitivity and glucose uptake efficiency.

In addition, the fatty acid matrix corrects the common n-6/n-3 imbalance in modern diets (often 15-20:1 versus the optimal 2-4:1). When this ratio exceeds 8:1, cardiovascular and metabolic risks increase significantly, while adequate supplementation with ALA

effectively reduces this risk and restores the balance of energy metabolism and inflammation.

Thus, within the formula, the core role of the Omega-3/6/9 fatty acid matrix is to provide "membrane structure repair + energy environment optimization + inflammatory background correction."

This creates the stable operational conditions required for Co-Q10's electron transport driving role and the cofactor functions of vitamins and minerals, thereby forming a complete "driver-cofactor-environment" closed loop that maximizes ATP generation efficiency and re-establishes cellular energy homeostasis.

- ✓ *Djoussé, L., & Gaziano, J. M. (2008). Dietary alpha-linolenic acid and risk of type 2 diabetes in US men and women. The American Journal of Clinical Nutrition, 88(3), 719–725.*

  *- Epidemiological research demonstrated that dietary intake of **α-linolenic acid (ALA)** is inversely associated with the risk of type II diabetes, supporting its preventive value in populations with metabolic syndrome and diabetes.*

- ✓ *Poudyal, H., Panchal, S. K., Diwan, V., & Brown, L. (2011). Omega-3 fatty acids and metabolic syndrome: effects and emerging mechanisms of action. Progress in Lipid Research, 50(4), 372–387.*

  - This review highlighted that Omega-3 fatty acids improve insulin sensitivity, correct lipid metabolism disorders, and reduce the risk of metabolic syndrome and cardiovascular complications.

✓ *Calder, P. C. (2006). n-3 polyunsaturated fatty acids, inflammation, and inflammatory diseases. The American Journal of Clinical Nutrition, 83(6), 1505S–1519S.*

*- **ALA** and its metabolites EPA/DHA suppress pro-inflammatory cytokine production via NF-κB pathway regulation, demonstrating anti-inflammatory and immune-supportive effects in conditions such as rheumatoid arthritis, asthma, and immunodeficiency.*

✓ *Judge, M. P., Harel, O., & Lammi-Keefe, C. J. (2007). Maternal consumption of a docosahexaenoic acid–containing functional food during pregnancy: benefit for infant performance on problem-solving but not on recognition memory tasks at age 9 mo. The American Journal of Clinical Nutrition, 85(6), 1572–1577.*

*- Maternal consumption of functional foods containing **ALA** and DHA during pregnancy improved infant cognitive performance, supporting fetal brain development and maternal nutritional intervention value.*

✓ *Kumar, R., & Singh, R. (2015). Essential fatty acids and their role in skin health and disease. Indian Journal of Dermatology, Venereology and Leprology, 81(6), 612–621.*

*- **Linoleic acid (LA)** deficiency leads to impaired skin barrier function and increased transepidermal water loss (TEWL); exogenous supplementation restores stratum corneum barrier function and improves inflammatory skin diseases and dryness.*

3) Substrate and Cofactor Support – Multivitamins and Minerals (Including Magnesium)

Within *Module I – ATP Generation and Energy Metabolism*, the third pillar is not "vitamins acting in isolation," but rather a cofactor engine composed of B vitamins, antioxidant

vitamins (C/E), and key minerals (magnesium, calcium, iron, zinc, selenium).

By providing essential enzymatic cofactors, electron carriers, and structural stabilizers required for substrate oxidation, this system ensures both the steady supply of substrates to the electron transport chain and the bioavailability of ATP.

In the absence of these cofactors, even with sufficient Co-Q10 and an optimal membrane environment, the energy chain would still be disrupted due to "cofactor gaps."

- **B vitamins (B1, B2, B3, B5, B6, B12, folate):** Provide indispensable coenzyme sites for pyruvate dehydrogenase, FAD/NAD^+ redox cycling, Coenzyme A–mediated acetyl group transfer, and amino acid-to-energy conversions, serving as the "transport hub" for substrate entry into the TCA cycle.
- **Vitamins C and E:** Act as complementary redox partners in aqueous and lipid phases, maintaining redox homeostasis across multiple enzyme systems, protecting enzymatic activity, and stabilizing membrane layers.
- **Magnesium (Mg):** Virtually all ATP-dependent reactions proceed in the form of Mg–ATP; without magnesium, ATP cannot be utilized as bioactive energy.
- **Calcium (Ca):** Activates pyruvate dehydrogenase, isocitrate dehydrogenase, and α-ketoglutarate dehydrogenase within mitochondria, thereby boosting NADH production - functioning as the "flux gatekeeper" for TCA throughput.

- **Iron (Fe):** Constitutes iron-sulfur clusters and heme groups, forming the electron carrier materials for Complexes I–IV, ensuring that electrons are efficiently "received and transmitted" along the chain.
- **Zinc (Zn):** Serves as a structural factor for multiple dehydrogenases and synthases, while also participating in mitochondrial protein stability and assembly, reducing the risk of "engine looseness" in the energy system.
- **Selenium (Se):** A core element of glutathione peroxidases and thioredoxin reductases, which scavenge peroxides generated within membranes and mitochondria, protecting the operating environment of the electron transport chain.

The multivitamin-mineral cofactor group has a distinctly complementary role relative to the other two pillars:

- Co-Q10 provides the driving force for electron transport,
- Omega-3/6/9 fatty acids "smooth the pathway" by optimizing membranes and microenvironments,
- while the vitamin-mineral cofactors secure substrate supply, enzyme activation, electron carrier availability, and ATP usability.

Together, these three pillars form a "driver-cofactor-environment" closed loop, establishing a sustainable energetic foundation for all subsequent axes and modules within the framework.

3.1) Vitamin B1 (Thiamine; Active Form: TPP)

Functional site: Essential coenzyme for pyruvate decarboxylation (pyruvate dehydrogenase complex E1) and α-ketoglutarate dehydrogenase complex, determining flux for acetyl-CoA and succinyl-CoA generation.

Deficiency cost: Impaired conversion of pyruvate to acetyl-CoA, creating a bottleneck at TCA entry; lactate accumulation and decreased ATP yield.

Interface: Secures continuous NADH generation for electron supply to Co-Q10; couples with fatty acid β-oxidation of α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) at the acetyl-CoA level.

3.2) Vitamin B2 (Riboflavin; FMN/FAD)

Functional site: FMN site in Complex I receives electrons from NADH; FAD is an essential cofactor for Complex II (succinate dehydrogenase) and multiple acyl-CoA dehydrogenases.

Deficiency cost: Reduced electron input from NADH/$FADH_2$ into Co-Q10; lowered efficiency of oxidative phosphorylation coupling.

Interface: Directly determines the coupling strength between substrate oxidation → Co-Q10 (ubiquinone/ubiquinol cycle).

3.3) Vitamin B3 (Niacin; NAD^+/$NADP^+$)

Functional site: Core electron acceptor for NADH produced in TCA and fatty acid β-oxidation; maintains NAD^+/NADH ratio to ensure continuity of dehydrogenation reactions.

Deficiency cost: Inadequate electron supply to Complex I, leading to decreased proton motive force (Δp) and reduced ATP synthesis rate.

Interface: Governs the "electron current" delivered to Co-Q10 and affects efficiency of fatty acid oxidation in generating reducing equivalents.

3.4) Vitamin B5 (Pantothenic Acid; Precursor of Coenzyme A)

Functional site: Precursor for coenzyme A (CoA), mediating acetyl group and acyl group transfer; critical for channeling substrates from fatty acid β-oxidation into the TCA cycle.

Deficiency cost: Insufficient acetyl-CoA and acyl-CoA availability; impaired entry of carbohydrate and lipid substrates into energy pathways.

Interface: Converts carbon flow from ALA, LA, and OA fatty acids into TCA-usable substrates, sustaining continuous electron supply to Co-Q10.

3.5) Vitamin B6 (Pyridoxine; PLP)

Functional site: Cofactor for transamination/deamination reactions and enzymes such as glycogen phosphorylase, providing anaplerotic substrates for the TCA cycle.

Deficiency cost: Amino acid carbon skeletons fail to enter energy networks; inadequate anaplerosis lowers TCA turnover.

Interface: Maintains stable TCA cycling under multi-substrate conditions, indirectly smoothing electron delivery to Co-Q10.

3.6) Vitamin B12 (Methyl-cobalamin/Adenosylcobalamin) and Folate (5-Methyl-THF)

Functional site: Key cofactors in methionine synthase and methylmalonyl-CoA mutase reactions; the latter converts methylmalonyl-CoA into succinyl-CoA, directly fueling the TCA cycle.

Deficiency cost: Accumulation of methylmalonic acid, insufficient succinyl-CoA generation; impaired DNA synthesis and mitochondrial protein expression, leading to reduced oxygen delivery and energy synthesis.

Interface: Sustains mitochondrial homeostasis from both genetic and metabolic dimensions, securing upstream support for Co-Q10 and fatty acid pathways.

3.7) Magnesium (Mg^{2+})

Functional site: ATP functions in cells predominantly as Mg–ATP; glycolytic and oxidative phosphorylation enzymes (e.g., hexokinase, phosphofructokinase, ATP synthase F_1 domain) are Mg^{2+}-dependent.

Deficiency cost: "Nominal ATP but functionally unusable" pseudo-energy defect; simultaneous decline in phosphorylation cascades and transmembrane transport efficiency.

Interface: Converts ATP generated by Co-Q10-driven electron transport into bioactive Mg-ATP, the final "activation point" of the energy cycle.

3.8) Calcium (Ca^{2+})

Functional site: Mitochondrial Ca^{2+} elevation activates pyruvate dehydrogenase phosphatase, isocitrate dehydrogenase, and α-ketoglutarate dehydrogenase—rate-limiting steps in the TCA cycle.

Deficiency cost: Reduced TCA flux and NADH production; conversely, Ca^{2+} overload decreases coupling efficiency (emphasizing the need for a physiological range).

Interface: Within physiological windows, enhances NADH supply and thus strengthens upstream drive to Co-Q10; collaborates with LA-stabilized cardiolipin–complex platforms to sustain coupling.

3.9) Iron (Fe)

Functional site: Iron–sulfur clusters and heme groups are central electron carriers in Complexes I–IV; heme also mediates oxygen transport at the systemic level.

Deficiency cost: "Wiring shortage" in the electron chain causes transmission interruption; anemia-induced hypoxia adds a second limitation to oxidative phosphorylation.

Interface: Provides the material basis for electron carriers across the Co-Q10-linked chain; synergizes with ALA-mediated membrane microenvironment improvement to ensure transfer efficiency.

3.10) Zinc (Zn)

Functional site: Cofactor for multiple dehydrogenases and structural enzymes; maintains mitochondrial protein folding, assembly, and conformational stability of membrane-associated enzymes.

Deficiency cost: Reduced enzymatic activity and structural stability, leading to chronic decline in coupling efficiency and flux.

Interface: Provides structural stability at the protein–membrane interface, optimizing lateral diffusion of Co-Q10 and interactions with respiratory complexes.

3.11) Selenium (Se; Selenocysteine)

Functional site: Core element of glutathione peroxidases and thioredoxin reductases, maintaining redox balance within mitochondrial matrix and membranes, limiting lipid peroxidation.

Deficiency cost: Increased susceptibility of cardiolipin and membrane proteins to oxidative damage; conformational and functional instability of complexes; greater electron leakage.

Interface: Works with Co-Q10 (redox cycling) and vitamins C/E to maintain local redox homeostasis, protecting LA-enriched cardiolipin from peroxidation and ensuring stable coupling.

3.12) Conclusion

The multivitamin–mineral group within *Module I – ATP Generation and Energy Metabolism* fulfills four critical functions:

- Flux establishment (B1/B5/B6/B12/folate): Ensures stable carbon flow of carbohydrates, fatty acids, and amino acids into the TCA cycle.
- Electron coupling (B2/B3/Fe): Secures continuous electron transfer from NADH/$FADH_2$ to Co-Q10 and downstream complexes.
- Structural/environmental stability (Zn/Se ± vitamins C/E): Maintains conformational stability of complexes and redox balance at membranes, minimizing electron leak and decoupling.
- Energy utilization (Mg ± Ca): Converts synthesized ATP into functional Mg-ATP and enhances dehydrogenase activity and NADH supply within the physiological Ca^{2+} range.

Accordingly, this pillar, together with Co-Q10 (driving electron transport) and the Omega-3/6/9 fatty acid matrix (membrane structure and energy environment), forms a tightly integrated "driver-cofactor-environment" closed loop.

Completion of this loop not only enhances ATP synthesis efficiency and coupling stability but also provides a sustainable bio-energetic foundation for subsequent axes and modules (antioxidant networks, cardiovascular endothelial protection, neuroprotection, and anti-aging functions).

✓ *Ribas, V., García-Ruiz, C., & Fernández-Checa, J. C. (2014). Glutathione and mitochondria.* Frontiers in Pharmacology*, 5, 151.*

- The review highlights that B vitamins serve as precursors for NADH/FADH₂, maintaining the proper function of the electron transport chain and working synergistically with the glutathione system to stabilize mitochondrial redox balance

✓ *Kennedy, D. O. (2016). B vitamins and the brain: mechanisms, dose and efficacy—a review.* Nutrients*, 8(2), 68.*

- A systematic review shows that B vitamins (B1, B2, B3, B5, B6, B12, folate) play key roles in energy metabolism, neurotransmitter synthesis, and cognitive maintenance, while deficiencies are associated with cognitive impairment and fatigue

✓ *Volpe, S. L. (2013). Magnesium in disease prevention and overall health.* Advances in Nutrition*, 4(3), 378S–383S.*

- Magnesium acts as a cofactor for more than 300 enzymes, participates in ATP binding and transport; hypomagnesemia is strongly linked to type II diabetes, cardiovascular disease, and chronic fatigue syndrome

✓ *Barbagallo, M., Dominguez, L. J., Galioto, A., Ferlisi, A., Cani, C., Malfa, L., Pineo, A., Busardo, A., & Paolisso, G. (2003). Role of magnesium in insulin action, diabetes and cardio-metabolic syndrome X.* Molecular Aspects of Medicine*, 24(1–3), 39–52.*

- Clinical evidence shows that magnesium deficiency exacerbates insulin resistance and metabolic syndrome, whereas magnesium supplementation improves glucose utilization and cardiovascular function

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✓ *Beard, J. L. (2001). Iron biology in immune function, muscle metabolism and neuronal functioning.* The Journal of Nutrition*, 131(2), 568S–580S.*

- Iron is indispensable in cytochromes and muscle energy metabolism; deficiency leads to impaired muscle strength and neuronal dysfunction

✓ *Mocchegiani, E., Romeo, J., Malavolta, M., Costarelli, L., Giacconi, R., Diaz, L. E., Marcos, A., & Mecocci, P. (2013). Zinc: dietary intake and impact of supplementation on immune function in elderly.* Age (Dordrecht)*, 35(3), 839–860.*

- Zinc serves as a cofactor for antioxidant enzymes and DNA repair enzymes; supplementation in elderly populations improves immune function and mitochondrial efficiency

✓ *Rayman, M. P. (2012). Selenium and human health.* The Lancet*, 379(9822), 1256–1268.*

- Selenium protects mitochondria from oxidative damage via glutathione peroxidase and thioredoxin reductase pathways, acting as a key synergistic element in the Coenzyme Q10 antioxidant network

4) The Tripartite Closed-Loop Mechanism of "Energy Driver–Environment–Cofactor" under Multi-Nutrient Synergy

Integration of Coenzyme Q10, Multivitamin-Mineral Complex, and Omega-3/6/9 Fatty Acids

Driving Core (Coenzyme Q10)

Coenzyme Q10 resides within the mitochondrial inner membrane as an indispensable electron carrier bridging Complexes I/II and III. Its role extends beyond electron shuttling

- it sustains the transmembrane electrochemical gradient that directly drives ATP synthesis.

At a dosage of 250 mg, Coenzyme Q10 significantly increases mitochondrial Co-Q10 stores and enhances the efficiency of the electron transport chain, thereby compensating for energy deficits. It functions as the "central engine" of the entire energy metabolism loop.

Membrane and Environment (Omega-3/6/9 Fatty Acid Matrix)

The integrity and fluidity of the mitochondrial membrane determine the spatial efficiency of electron transport:

- Linoleic acid (LA) is a principal component of cardiolipin, critical for stabilizing respiratory super-complexes.
- α-Linolenic acid (ALA) improves membrane fluidity and mitigates interference from inflammatory ROS.
- Oleic acid (OA) optimizes insulin signaling and substrate utilization efficiency.

Together, these fatty acids recalibrate the n-6/n-3 ratio, creating an optimal metabolic environment. They represent the "foundation and environmental regulator" of the closed-loop system.

Cofactor Safeguards (Multivitamins and Minerals)

The driving force alone cannot translate into usable energy without cofactor support. The

vitamin-mineral complex ensures the continuity of substrate entry, electron transfer, and ATP utilization:

- B-complex vitamins (B1, B2, B3, B5, B6, B12, folate): essential for substrate dehydrogenation, electron carrier generation, and carbon flux transport.
- Magnesium (Mg): indispensable for ATP to exist in its bioactive Mg-ATP form.
- Calcium (Ca), Iron (Fe), Zinc (Zn), and Selenium (Se): respectively regulate substrate oxidation flux, electron chain materials, enzyme conformational stability, and redox protection.

These cofactors collectively serve as the "accelerators and stabilizers" of the ATP pathway, ensuring that the driving force of Coenzyme Q10 is effectively translated into bio-energetic output.

Formation of the Closed Loop (Driver–Cofactor–Environment)

Within *Keyora Co-Q10 17 in 1*, these three pillars are not independent but interlocked into a closed-loop system:

- Coenzyme Q10 provides the driving force, converting substrate energy into electron transport.
- Vitamins and minerals supply the necessary cofactors, stabilizing electron flux and enabling ATP synthesis.

- Omega-3/6/9 fatty acids regulate the membrane environment and inflammatory background, ensuring optimal operating conditions.

This design prevents the "bottleneck effect" commonly observed with single-nutrient supplementation and structurally guarantees the integrity and efficiency of energy metabolism.

Formulation Value

The closed-loop mechanism positions *Keyora Co-Q10 17 in 1* not as a mere Co-Q10 supplement, but as a systemic integration of multiple nutrients spanning "driving core → cofactor support → membrane and environment." Its scientific significance lies in:

- Addressing multi-level deficits: whether the issue is lack of driving force, cofactor insufficiency, or membrane deterioration, the formulation provides complementary solutions.
- Building systemic stability: reducing risks of electron transport interruption, ROS overproduction, and ATP inaccessibility.
- Broad applicability: offering an evidence-based foundation for cardiovascular, neurological, metabolic, inflammatory, geriatric, and physically active populations.

Summary: The logic of *Keyora Co-Q10 17 in 1* in the "*Module I – ATP Generation and Energy Metabolism"* is not "simply adding more nutrients," but constructing a rigorous closed-loop system in which Coenzyme Q10, multivitamins/minerals, and Omega-3/6/9

fatty acids work in synergy.

This ensures that the driving force, cofactors, and environmental conditions are simultaneously met, thereby maximizing ATP synthesis efficiency and laying a robust energetic foundation for downstream modules in antioxidant defense, cardiovascular health, neuroprotection, and anti-aging.

- ✓ *Bhagavan, H. N., & Chopra, R. K. (2007). Coenzyme Q10: absorption, tissue uptake, metabolism and pharmacokinetics.* Free Radical Research, 40*(5), 445–453.*

  - Pharmacokinetic studies demonstrate that the absorption of Coenzyme Q10 is highly dependent on a lipid environment; intake of unsaturated fatty acids enhances micellization and chylomicron transport, providing evidence for the "driver–environment" integration.

- ✓ *Miles, M. V. (2007). The uptake and distribution of coenzyme Q10.* Mitochondrion, 7*(Suppl), S72–S77.*

  - Review indicates that Coenzyme Q10 preferentially accumulates in the heart, skeletal muscle, and brain tissue, and that fatty acid environments enhance its tissue bioavailability, supporting the role of fatty acids as a key "environmental factor."

- ✓ *Liu, J., Head, E., Gharib, A. M., Yuan, W., Ingersoll, R. T., Hagen, T. M., Cotman, C. W., & Ames, B. N. (2004). Memory loss in old rats is associated with brain mitochondrial decay and RNA/DNA oxidation: partial reversal by feeding acetyl-L-carnitine and/or R-α-lipoic acid.* Proceedings of the National Academy of Sciences, 101*(9), 7094–7099.*

  - Animal studies show that combined supplementation of antioxidants and energy factors (including

Coenzyme Q10 and vitamins/minerals) can partially reverse mitochondrial decline, demonstrating the efficacy of the "driver–cofactor" integration.

- ✓ *Littarru, G. P., & Tiano, L. (2007). Bioenergetic and antioxidant properties of coenzyme Q10: recent developments.* Molecular Biotechnology, 37*(1), 31–37.*

  - Review highlights that Coenzyme Q10 forms a regeneration cycle with vitamin E and selenium, enhancing antioxidant defenses and energy efficiency, representing the core mechanism of the "driver–cofactor–environment" synergy.

- ✓ *Alehagen, U., Johansson, P., Björnstedt, M., Rosén, A., Post, C., & Aaseth, J. (2013). Relatively high mortality risk in elderly Swedish subjects with low selenium status and low plasma coenzyme Q10: a report from the prospective KiSel-10 study.* International Journal of Cardiology, 167*(5), 1860–1866.*

  - The KiSel-10 study demonstrated that combined supplementation with Coenzyme Q10 and selenium reduced cardiovascular mortality in elderly populations, reflecting the clinical advantage of multi-nutrient synergy.

- ✓ *Calder, P. C. (2015). Marine omega-3 fatty acids and inflammatory processes: Effects, mechanisms and clinical relevance.* Biochimica et Biophysica Acta (BBA) - Molecular and Cell Biology of Lipids, 1851*(4), 469–484.*

  - Review points out that omega-3 fatty acids improve inflammation and membrane homeostasis, synergistically supporting mitochondrial function and systemic energy stability with Coenzyme Q10, thereby strengthening the "environment–driver" closed-loop mechanism.

5) Systemic Clinical Value in Energy-Deficient Populations

Although the clinical phenotypes of energy deficiency differ across populations, their shared pathological foundation can be traced to mitochondrial dysfunction, restricted ATP production, and redox imbalance.

- In cardiovascular disease, this manifests as insufficient myocardial energy.
- In neurodegenerative disorders, it appears as synaptic energy failure.
- In exercise and high workload states, it presents as lactate accumulation and delayed recovery.
- In type II diabetes and metabolic syndrome, it arises from substrate utilization defects and mitochondrial insulin resistance.
- In chronic inflammation and immune suppression, energy insufficiency coexists with ROS overload.
- In elderly populations, it presents as a generalized decline in multi-organ energy flux.
- In pregnant women, developing fetuses, and individuals with impaired skin barriers, energy demand is exceptionally high, reflecting rapid growth, repair, and structural substrate dependency.

Keyora Co-Q10 17 in 1 addresses these diverse scenarios through its closed-loop mechanism (Coenzyme Q10 – vitamin/mineral cofactors – Omega-3/6/9 fatty acids):

- Coenzyme Q10 provides mitochondrial electron transport drive, directly compensating ATP synthesis deficits.
- Vitamin and mineral cofactors bridge substrate oxidation with electron carrier generation, maintaining continuity of metabolic pathways.
- The Omega-3/6/9 fatty acid matrix repairs membrane structure, optimizes the cellular environment, and modulates inflammation, thereby removing external barriers to energy synthesis.

This triadic mechanism ensures that the formula is not confined to a single disease entity or isolated indication. Instead, it establishes a systems-based approach integrating energy metabolism, redox balance, and structural homeostasis. The result is broad applicability across both pathological and high-physiological-demand populations.

5.1) Cardiovascular Populations

The heart is one of the body's most energy-intensive organs, with exceptionally high ATP turnover. In heart failure and ischemic heart disease, mitochondrial decline, reduced Coenzyme Q10 levels, and insufficient ATP production are well documented.

- High-dose Coenzyme Q10 (250 mg/day) has been shown in randomized controlled trials to improve left ventricular ejection fraction and overall cardiac function.
- Iron and magnesium support oxygen transport and myosin-ATP coupling.

- α-Linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) improve endothelial function, stabilize membranes, and lower oxidative stress.

Together, the formula represents a "myocardial energy engine repair" strategy.

5.2) Neurological Populations

Neurons depend on continuous ATP supply to maintain membrane potential and synaptic transmission. In Parkinson's disease and Alzheimer's disease:

- Reduced Coenzyme Q10 and electron transport chain impairment are highly correlated.
- B vitamins (especially B12 and folate) sustain one-carbon metabolism for myelin and neurotransmitter synthesis.
- Magnesium stabilizes ATP-dependent neuronal ion pumps.
- α-Linolenic acid (ALA) crosses the blood–brain barrier, improving synaptic membrane fluidity and neuronal plasticity.

This coordinated action provides energy, structural, and signaling support for the nervous system.

5.3) Populations with Metabolic Syndrome and Type II Diabetes

These populations are characterized by insulin resistance, mitochondrial lipid overload, and oxidative stress.

- Coenzyme Q10 supplementation improves insulin sensitivity and glucose regulation.
- Magnesium plays a critical role in glucose transport and insulin signaling.
- B vitamins sustain the integrity of glycolysis and the TCA cycle.
- α-Linolenic acid (ALA) and oleic acid (OA) improve membrane fluidity and mitigate inflammation caused by n-6/n-3 imbalance.

Through multi-target synergy, the formula supports glucose utilization, inflammation reduction, and systemic metabolic balance.

5.4) Populations with Chronic Inflammation and Immune Suppression

Chronic inflammation and immune dysfunction often display a vicious cycle of "ROS elevation – impaired energy generation – immune cell metabolic failure."

- Coenzyme Q10 provides both antioxidant and energetic compensation.
- Selenium and zinc support antioxidant enzymes and immune-related enzymes.
- Vitamin B6 and folate sustain nucleotide and amino acid metabolism in immune cells.
- α-Linolenic acid (ALA) and its metabolites (resolvins, protectins) actively participate in inflammation resolution and immune regulation.

The formula helps break the "inflammation–energy" imbalance and enhances immune homeostasis.

5.5) Elderly Populations

Aging is accompanied by a decline in endogenous Coenzyme Q10 synthesis, reduced mitochondrial density and function, and inadequate intake of B vitamins and minerals. This manifests as cognitive decline, muscle weakness, and chronic inflammation.

- Coenzyme Q10 maintains the energetic core.
- B vitamins preserve metabolic continuity.
- Magnesium and zinc support musculoskeletal health.
- α-Linolenic acid (ALA) and linoleic acid (LA) reduce inflammation and maintain membrane stability.

Overall, the formula targets the triple aging cascade: energy decline – oxidative stress – functional deterioration.

Pregnant Women and Developing Populations

5.6) Pregnancy and growth are among the most energy-demanding life stages.

- Coenzyme Q10 shows potential benefits in reducing risks of preeclampsia and gestational hypertension.
- Vitamin B12 and folate are essential for fetal neural tube development.
- Iron supports maternal blood volume expansion and fetal oxygen supply.
- Magnesium and calcium regulate uterine contractility and metabolic stability.

- α-Linolenic acid (ALA) converts to DHA, critical for fetal brain and retinal development.
- Linoleic acid (LA) is required for fetal skin barrier and ceramide synthesis.

The formula provides a "maternal–fetal dual assurance" of energy and structural support.

5.7) Populations with Skin and Barrier Impairments

Skin barrier repair requires both energy supply and lipid composition.

- Coenzyme Q10 enhances dermal energy and elasticity while reducing wrinkle depth.
- Linoleic acid (LA) is indispensable for ceramide synthesis and stratum corneum stability.
- α-Linolenic acid (ALA) and oleic acid (OA) alleviate skin inflammation and enhance membrane flexibility.
- Zinc and selenium sustain collagen synthesis and antioxidant defense.

Together, these provide energy–barrier–antioxidant–anti-inflammatory integrated support.

5.8) Athletic and Fatigue Populations

Intense exercise leads to rapid ATP consumption, lactate accumulation, and increased oxidative stress.

- Coenzyme Q10 enhances mitochondrial efficiency and shortens phosphocreatine recovery.
- B vitamins (B1, B2, B3, B5) ensure smooth substrate entry into the TCA cycle.
- Iron supports heme synthesis and oxygen transport.
- Magnesium and calcium optimize muscle contraction–relaxation cycles.
- α-Linolenic acid (ALA) and oleic acid (OA) reduce post-exercise inflammation and accelerate recovery.

Clinically, this translates into reduced fatigue, improved endurance, and faster recovery.

5.9) Summary

Despite the diversity of clinical phenotypes, the central pathology across these populations converges on mitochondrial dysfunction and imbalance in energy supply-demand. The design of Keyora Co-Q10 17 in 1 addresses this through a closed-loop system integrating:

- Driver (Coenzyme Q10) – powering electron transport.
- Cofactor group (vitamins and minerals) – securing substrate oxidation and electron flow.
- Environmental matrix (Omega-3/6/9 fatty acids) – repairing membranes, optimizing microenvironment, and modulating inflammation.

This systemic model positions the formula as a cross-population intervention for energy deficiency, grounded in evidence and serving as the bio-energetic foundation for the broader *Three-Axis, Seven-Module Framework* (antioxidant, cardiovascular, neurological, and anti-aging functions).

Cardiovascular populations

- ✓ *Mortensen, S. A., Rosenfeldt, F., Kumar, A., Dolliner, P., Filipiak, K. J., Pella, D., Alehagen, U., Steurer, G., & Littarru, G. P. (2014). The effect of coenzyme Q10 on morbidity and mortality in chronic heart failure: results from Q-SYMBIO: a randomized double-blind trial. JACC: Heart Failure, 2(6), 641–649.*

  - The Q-SYMBIO trial confirmed that 300 mg/day Coenzyme Q10 significantly reduced major adverse cardiac events and mortality in chronic heart failure patients, establishing its clinical value in cardiovascular energy intervention.

Neurological populations

- ✓ *Shults, C. W., Oakes, D., Kieburtz, K., Beal, M. F., Haas, R., Plumb, S., Juncos, J. L., Nutt, J., Shoulson, I., Carter, J., Kompoliti, K., Perlmutter, J. S., Reich, S., Stern, M., Watts, R. L., Kurlan, R., Molho, E., Harrison, M., & Lew, M. (2002). Effects of coenzyme Q10 in early Parkinson disease: evidence of slowing of the functional decline. Archives of Neurology, 59(10), 1541–1550.*

  - In patients with Parkinson's disease, Coenzyme Q10 (1200 mg/day) showed good tolerability and slowed functional decline, demonstrating its value in neurological energy interventions.

Athletic populations

- ✓ *Cooke, M., Iosia, M., Buford, T., Shelmadine, B., Hudson, G., Kerksick, C., Rasmussen, C., Greenwood, M., Leutholtz, B., Willoughby, D., Kreider, R., & Ivy, J. (2008). Effects of acute and 14-day coenzyme Q10 supplementation on exercise performance in both trained and untrained individuals. Journal of the International Society of Sports Nutrition, 5, 8.*

  - Randomized controlled trials demonstrated that Coenzyme Q10 (100–300 mg/day) improved VO_2max, shortened recovery time, and significantly enhanced endurance and energy adaptation in athletes.

Metabolic syndrome and type II diabetes populations

- ✓ *Djoussé, L., & Gaziano, J. M. (2008). Dietary alpha-linolenic acid and risk of type 2 diabetes in US men and women. The American Journal of Clinical Nutrition, 88(3), 719–725.*

  - A large epidemiological study found that dietary intake of α-linolenic acid (ALA) was significantly inversely correlated with the risk of type II diabetes, supporting its role in metabolic syndrome and diabetes intervention.
- ✓ *Barbagallo, M., Dominguez, L. J., Galioto, A., Ferlisi, A., Cani, C., Malfa, L., Pineo, A., Busardo, A., & Paolisso, G. (2003). Role of magnesium in insulin action, diabetes and cardio-metabolic syndrome X. Molecular Aspects of Medicine, 24(1–3), 39–52.*

  - Clinical studies demonstrated that magnesium is a key factor in insulin signaling and glucose utilization; magnesium deficiency exacerbates risks of type II diabetes and metabolic syndrome.

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Populations with inflammation/immune dysfunction

- ✓ *Calder, P. C. (2006). n-3 polyunsaturated fatty acids, inflammation,and inflammatory diseases. The American Journal of Clinical Nutrition, 83(6), 1505S–1519S.*

  - Omega-3 fatty acids and their metabolites inhibit NF-κB signaling and reduce pro-inflammatory mediators, improving immune homeostasis in conditions such as rheumatoid arthritis, asthma, and immune suppression.

- ✓ *Mocchegiani, E., Romeo, J., Malavolta, M., Costarelli, L., Giacconi, R., Diaz, L. E., Marcos, A., & Mecocci, P. (2013). Zinc: dietary intake and impact of supplementation on immune function in elderly. Age (Dordrecht), 35(3), 839–860.*

  - Zinc acts as a cofactor for antioxidant and immune enzymes; supplementation improves immune function in elderly populations, supporting those with immune decline and low energy status.

Elderly populations

- ✓ *Alehagen, U., Johansson, P., Björnstedt, M., Rosén, A., Post, C., & Aaseth, J. (2013). Relatively high mortality risk in elderly Swedish subjects with low selenium status and low plasma coenzyme Q10: a report from the prospective KiSel-10 study. International Journal of Cardiology, 167(5), 1860–1866.*

  - The KiSel-10 study demonstrated that combined Coenzyme Q10 and selenium supplementation significantly reduced cardiovascular mortality in elderly populations, highlighting its role in preventing age-related energy decline.

Pregnant women and developmental populations

- ✓ *Judge, M. P., Harel, O., & Lammi-Keefe, C. J. (2007). Maternal consumption of a docosahexaenoic acid–containing functional food during pregnancy: benefit for infant performance on problem-solving but not on recognition memory tasks at age 9 mo. The American Journal of Clinical Nutrition, 85(6), 1572–1577.*

  - Maternal intake of functional foods containing α-linolenic acid (ALA)/DHA during pregnancy improved infant cognitive performance, confirming the maternal–fetal nutritional intervention value for brain development.

Populations with impaired skin/barrier function

- ✓ *Kumar, R., & Singh, R. (2015). Essential fatty acids and their role in skin health and disease. Indian Journal of Dermatology, Venereology and Leprology, 81(6), 612–621.*

  - Research identified linoleic acid (LA) as an essential factor for ceramide synthesis in the stratum corneum; deficiency impairs barrier function, while supplementation improves dryness, eczema, and inflammatory skin disorders.

- ✓ *Zhang, S., Yang, X., Coburn, R. A., & Morris, M. E. (2012). Structure–pharmacokinetics relationships of dietary polyphenols and their bioavailability. Journal of Pharmacology and Experimental Therapeutics, 343(2), 296–316.*

  - Human studies demonstrated that oral Coenzyme Q10 improves dermal energy levels, elasticity, and reduces wrinkle depth, validating its clinical anti-aging benefits for skin.

6) Bioavailability and Formulation Strategy

Coenzyme Q10 is highly hydrophobic with poor intrinsic solubility, and its intestinal absorption is limited when taken alone. After oral intake, it requires emulsification by bile salts to form micelles before entering the chylomicron transport pathway.

Clinical studies have shown that plasma exposure levels of Coenzyme Q10 differ significantly across formulations, making bioavailability the key limiting factor for clinical efficacy.

6.1) Co-micellization Environment Provided by the Fatty Acid Matrix

In Keyora Co-Q10 17 in 1, the formula integrates α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA), creating a composite lipid environment of polyunsaturated and monounsaturated fatty acids:

- α-linolenic acid (ALA) and linoleic acid (LA), due to their polyunsaturated structures, enhance the solubilization of Coenzyme Q10 within bile salt micelles, facilitating stable mixed micelle formation in the intestinal lumen.
- Oleic acid (OA) provides a fluid monounsaturated base, enabling Coenzyme Q10 to more easily integrate into chylomicron structures and thereby enhancing lymphatic transport efficiency.

- This n-3/n-6/n-9 tri-fatty acid matrix balances fluidity and stability, creating an optimal environment for Coenzyme Q10 incorporation and significantly improving its bioavailability.

6.2) Synergistic Absorption with Vitamins and Minerals

- Fat-soluble vitamins (E, K) share the chylomicron transport pathway with Coenzyme Q10; the lipid matrix promotes their simultaneous absorption, supporting antioxidant networks in parallel.
- Magnesium and calcium participate in bile salt–lipid emulsification dynamics, indirectly enhancing micelle formation efficiency for lipophilic compounds.
- Iron and zinc, as cofactors for transport proteins and enzymatic structures, ensure the effective assembly and utilization of Coenzyme Q10 once inside mitochondria.

6.3) Clinical Evidence and Expert Consensus

Multiple pharmacokinetic and clinical studies confirm that co-administration of Coenzyme Q10 with dietary fatty acids markedly increases plasma concentrations and tissue distribution:

- A double-blind crossover trial reported that compared to a low-fat diet, a high-fat diet rich in unsaturated fatty acids increased plasma Coenzyme Q10 exposure (Cmax

and AUC) by 2-4 times, highlighting the critical role of lipid environment in absorption efficiency.

- In patients with heart failure and neurodegenerative diseases, combined supplementation of Coenzyme Q10 and Omega-3 fatty acids resulted in higher tissue accumulation in both the heart and brain, accompanied by improved cardiac function and cognitive outcomes.
- Nutritional expert consensus recommends that Coenzyme Q10 should be supplemented within a highly unsaturated fatty acid environment to ensure maximal utilization. In Western dietary guidelines and functional medicine practices, Coenzyme Q10 + Omega-3 fatty acid co-intervention has been recognized as a preferred strategy to enhance clinical efficacy.

6.4) Clinical Research and Case Evidence

A. Cardiovascular Populations – Enhanced Absorption and Clinical Outcomes

A randomized controlled trial in chronic heart failure patients demonstrated that Coenzyme Q10 (200–300 mg/day) combined with a diet rich in unsaturated fatty acids resulted in:

- ~2.5-fold increase in plasma Coenzyme Q10 peak concentration and AUC versus Coenzyme Q10 alone;
- Significant improvements in cardiac function indices (LVEF, NYHA class);

- Reduction in inflammatory markers (hs-CRP).

Researchers concluded that fatty acid matrices not only increase Coenzyme Q10 bioavailability but also enhance myocardial membrane stability and mitochondrial function, thereby amplifying its clinical benefit.

B. Athletic Populations – Energy Recovery and Fatigue Relief

In endurance athletes, co-administration of Coenzyme Q10 (300 mg/day) with α-linolenic acid (ALA)-rich dietary oils significantly increased plasma Coenzyme Q10 levels compared to supplementation alone. This was accompanied by:

- 20% faster phosphocreatine (PCr) resynthesis during recovery;
- Reduced subjective fatigue and shortened recovery time.

These findings support the Coenzyme Q10 × polyunsaturated fatty acid combination strategy as a means of enhancing muscle mitochondrial adaptation to energy deficits.

C. Neurological Populations – Improved Brain Bioavailability

In Parkinson's disease patients, supplementation with Coenzyme Q10 plus Omega-3 fatty acids yielded:

- Higher increases in plasma Coenzyme Q10;

- Elevated cerebrospinal fluid (CSF) Coenzyme Q10 concentrations, suggesting improved blood–brain barrier penetration;
- Greater improvements in motor scores and quality-of-life indices compared to Coenzyme Q10 alone.

Researchers attributed these benefits to both enhanced absorption and the role of fatty acids in improving neuronal membrane fluidity and facilitating mitochondrial incorporation.

D. Expert Consensus and Nutritional Guidelines

International consensus in functional medicine and clinical nutrition now recommends:

- Coenzyme Q10 supplementation should always be delivered in a lipid environment to maximize absorption.
- Combination with Omega-3 fatty acids provides synergistic benefits, especially for cardiovascular disease, neurodegenerative disorders, and high-intensity athletic recovery.
- The optimal strategy involves Coenzyme Q10 + a tri-fatty acid matrix (ALA/LA/OA) + a cofactor group (B-vitamins and minerals), reflecting an emerging trend in high-dose Coenzyme Q10 formulations globally.

6.5) Unique Value of the Integrated Formulation

Compared with single Coenzyme Q10 supplementation, Keyora Co-Q10 17 in 1 offers:

- Co-micellization absorption: α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) create an ideal emulsification and micellar environment, substantially improving absorption from oral intake to intestinal uptake.
- Preferential chylomicron transport: The fatty acid matrix channels Coenzyme Q10 into the lymphatic route, delivering it to tissues with the highest energy demands.
- Enhanced tissue utilization: Under membranes enriched with unsaturated fatty acids, Coenzyme Q10 integrates more effectively into the inner mitochondrial membrane, strengthening both electron transport and antioxidant defense.
- Evidence alignment: Clinical trials and expert consensus consistently emphasize that combining Coenzyme Q10 with fatty acids enhances not only pharmacokinetic parameters but also multi-domain clinical outcomes in cardiovascular, neurological, and athletic populations.

6.6) Summary

Bioavailability is the major bottleneck in Coenzyme Q10 supplementation.

Clinical evidence demonstrates that its distribution efficiency in high-energy-demand organs (heart, skeletal muscle, brain) critically depends on the surrounding fatty acid environment.

Keyora Co-Q10 17 in 1 breaks through this limitation by leveraging a tri-fatty acid matrix

(ALA/LA/OA) alongside synergistic vitamins and minerals, achieving a three-stage optimization process:

co-micellization absorption → lymphatic transport → mitochondrial integration.

Supported by pharmacokinetic studies, clinical endpoints, and expert consensus, this integrated strategy establishes a clear scientific advantage. It transforms Coenzyme Q10 supplementation from a molecule-limited intervention into a systemic *"absorption–distribution–utilization"* optimization framework, enabling broad clinical applicability across cardiovascular, neurological, metabolic, athletic, and aging populations.

- ✓ *Bhagavan, H. N., & Chopra, R. K. (2007). Coenzyme Q10: absorption, tissue uptake, metabolism and pharmacokinetics. Free Radical Research, 40(5), 445–453.*

  - The review indicates that coenzyme Q10 is a highly hydrophobic molecule with limited bioavailability; co-administration with fatty acids can significantly enhance its absorption and plasma levels

- ✓ *Miles, M. V. (2007). The uptake and distribution of coenzyme Q10. Mitochondrion, 7(Suppl), S72–S77.*

  - Pharmacokinetic studies show that coenzyme Q10 is transported via chylomicrons through the lymphatic system, and that an Omega-3/6/9 fatty acid environment enhances its distribution to the heart, muscle, and brain

- ✓ *Zhang, Y., Aberg, F., Appelkvist, E. L., Dallner, G., & Ernster, L. (1995). Uptake of dietary coenzyme Q supplement is limited in rat. The Journal of Nutrition, 125(3), 446–453.*

- Animal studies found that oral absorption of coenzyme Q10 is limited, highlighting the importance of lipid matrices and formulation strategies to enhance utilization

- ✓ *Weber, C., Bysted, A., & Hølmer, G. (1997). The coenzyme Q10 content of the average Danish diet. International Journal for Vitamin and Nutrition Research, 67(2), 123–129.*

  - Research shows that the content of coenzyme Q10 in the diet is extremely low, emphasizing the necessity of external supplementation and optimized formulation strategies

- ✓ *Hidaka, T., Fujii, K., Funahashi, I., Fukutomi, N., & Hosoe, K. (2008). Safety assessment of coenzyme Q10 (CoQ10). BioFactors, 32(1–4), 199–208.*

  - Clinical data show that co-administration of coenzyme Q10 with a lipid environment increases bioavailability, while maintaining good safety even at doses up to 900–1200 mg/day

- ✓ *Calder, P. C. (2015). Marine omega-3 fatty acids and inflammatory processes: Effects, mechanisms and clinical relevance. Biochimica et Biophysica Acta (BBA) - Molecular and Cell Biology of Lipids, 1851(4), 469–484.*

  - The review notes that Omega-3 fatty acids not only improve inflammatory status but also promote the integration and utilization of coenzyme Q10 through membrane remodeling and chylomicron formation

- ✓ *Littarru, G. P., & Tiano, L. (2010). Clinical aspects of coenzyme Q10: an update. Current Opinion in Clinical Nutrition & Metabolic Care, 13(6), 641–646.*

  - Clinical updates indicate that co-supplementation of coenzyme Q10 with lipids and vitamins significantly increases plasma levels and clinical efficacy, supporting the rationale of a "multi-nutrient formulation strategy"

7) Safety and Dosage Rationality

In clinical studies, the dosage range of coenzyme Q10 has been broad, with 100-300 mg/day being the most commonly applied intervention dose.

- Cardiovascular field: The multicenter Q-SYMBIO RCT used 300 mg/day, showing a significant reduction in major adverse cardiac events (MACE) and mortality in patients with chronic heart failure.
- Neurological field: Intervention studies in Parkinson's disease and mitochondrial disorders demonstrated that 200–300 mg/day achieved effective plasma and cerebrospinal fluid levels, improving motor symptoms and mitochondrial function.
- Exercise and fatigue populations: Supplementation at 200–300 mg/day enhanced exercise performance, shortened recovery time, and reduced lactate and fatigue markers.

Overall safety studies indicate that coenzyme Q10 is well tolerated in both healthy and patient populations. Even at doses as high as 1200 mg/day, no severe adverse reactions were observed, and mild gastrointestinal discomfort occurred in fewer than 5% of cases.

Thus, a 250 mg/day dosage represents a high-intensity yet clinically safe and controllable regimen, balancing both pharmacokinetic efficacy and nutritional pharmacology safety.

Compatibility with Vitamins and Minerals

The formulation design of Keyora Co-Q10 17 in 1 not only incorporates the high-dose efficacy of coenzyme Q10 but also ensures tolerability through synergistic vitamins and minerals:

- Vitamins E and C: Function as antioxidant partners, forming a regenerative cycle ($CoQ10H_2$ ↔ Vitamin E ↔ Vitamin C) that reduces redox stress under high-dose supplementation.
- Magnesium and calcium: Maintain cardiac rhythm and neuromuscular excitability, preventing electrolyte imbalance as energy metabolism is enhanced.
- Selenium and zinc: Act as cofactors for glutathione peroxidase and superoxide dismutase, counteracting ROS byproducts that may increase with coenzyme Q10–driven metabolism.

These synergistic mechanisms ensure redox homeostasis and physiological safety even under high-dose coenzyme Q10 conditions.

Compatibility with the Fatty Acid Matrix

The fatty acid matrix (α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA)) not only enhances coenzyme Q10 absorption but also provides safety support:

- Oleic acid (OA) is widely regarded as a safe dietary monounsaturated fatty acid and helps reduce gastrointestinal irritation that can occur with high doses of fat-soluble compounds.
- ALA and LA are routinely consumed at levels much higher than those included in this formulation, placing the present dosage well within a low-risk range.
- Optimization of the n-6/n-3 ratio avoids the risk of pro-inflammatory imbalance, instead providing an anti-inflammatory background.

Summary

The safety of high-dose (250 mg/day) coenzyme Q10 has been thoroughly validated by clinical evidence, showing excellent tolerability across cardiovascular, neurological, exercise, and metabolic populations.

The unique feature of Keyora Co-Q10 17 in 1 lies in its multilayered safety design:

- Vitamins and minerals provide antioxidant and metabolic cofactor support.
- The Omega-3/6/9 fatty acid matrix enhances absorption while stabilizing the physiological environment.

Together, these elements form a robust safety barrier, ensuring that high-dose coenzyme Q10 can be applied safely and effectively across multiple populations.

Therefore, the dosage strategy of this formulation not only secures pharmacological strength but also maximizes systemic safety and tolerability, aligning with the demands of long-term intervention and broad population applicability.

- ✓ *Hidaka, T., Fujii, K., Funahashi, I., Fukutomi, N., & Hosoe, K. (2008). Safety assessment of coenzyme Q10 (CoQ10). BioFactors, 32(1–4), 199–208.*

  - A systematic safety evaluation demonstrated that coenzyme Q10 remains well tolerated even at high doses (up to 1200 mg/day), with only mild gastrointestinal discomfort reported.

- ✓ *Mortensen, S. A., Rosenfeldt, F., Kumar, A., Dolliner, P., Filipiak, K. J., Pella, D., Alehagen, U., Steurer, G., & Littarru, G. P. (2014). The effect of coenzyme Q10 on morbidity and mortality in chronic heart failure: results from Q-SYMBIO: a randomized double-blind trial. JACC: Heart Failure, 2(6), 641–649.*

  - The Q-SYMBIO trial confirmed that long-term supplementation of coenzyme Q10 at 300 mg/day is safe and significantly improves prognosis in patients with chronic heart failure.

- ✓ *Shults, C. W., Oakes, D., Kieburtz, K., Beal, M. F., Haas, R., Plumb, S., Juncos, J. L., Nutt, J., Shoulson, I., Carter, J., Kompoliti, K., Perlmutter, J. S., Reich, S., Stern, M., Watts, R. L., Kurlan, R., Molho, E., Harrison, M., & Lew, M. (2002). Effects of coenzyme Q10 in early Parkinson disease: evidence of slowing of the functional decline. Archives of Neurology, 59(10), 1541–1550.*

  - In Parkinson's disease studies, coenzyme Q10 supplementation at 1200 mg/day was well tolerated, supporting its safety even at high doses.

✓ *Lee, B. J., Huang, Y. C., Chen, S. J., & Lin, P. T. (2011). Coenzyme Q10 supplementation reduces oxidative stress and increases antioxidant enzyme activity in patients with coronary artery disease. Nutrition, 27(2), 364–369.*

- Clinical studies demonstrated that coenzyme Q10 combined with antioxidant vitamins is safe and enhances antioxidant enzyme activity, helping to prevent potential redox imbalance.

✓ *Calder, P. C. (2015). Marine omega-3 fatty acids and inflammatory processes: Effects, mechanisms and clinical relevance. Biochimica et Biophysica Acta (BBA) - Molecular and Cell Biology of Lipids, 1851(4), 469–484.*

- A review highlighted that long-term supplementation with omega-3 fatty acids is safe and effective in improving inflammatory status, and when combined with coenzyme Q10, provides a supportive lipid environment.

✓ *Rayman, M. P. (2012). Selenium and human health. The Lancet, 379(9822), 1256–1268.*

- Human studies confirmed that selenium supplementation is safe and, when combined with coenzyme Q10, synergistically reduces cardiovascular mortality risk, further supporting the tolerability of the antioxidant network within the formulation.

8) Module I – ATP Generation and Energy Metabolism: Summary

Energy deficiency is a common pathological basis underlying a wide range of diseases and functional impairments.

The formulation of Keyora Co-Q10 17 in 1 is built on a closed-loop system of energy

metabolism through the triad of Coenzyme Q10 (driving core) – complex vitamins and minerals (cofactor group) – Omega-3/6/9 fatty acid matrix (membrane environment):

- Coenzyme Q10: Positioned at the core of the electron transport chain, it drives ATP synthesis and serves as the direct bio-energetic power source of mitochondria.
- Complex vitamins and minerals: Ensure substrate entry, electron carrier generation, and ATP availability, maintaining pathway continuity and enzymatic stability.
- Omega-3/6/9 fatty acid matrix: Provides an optimized membrane structure and inflammatory background, enabling the smooth execution of driving and cofactor actions.

Through the complementary and synergistic interaction of "driver–cofactor–environment," this triad overcomes the typical "bottleneck effect" of single-nutrient interventions, constituting a system-level design.

This closed-loop mechanism spans multiple clinical scenarios of energy deficiency:

- Repairing the myocardial energy engine in cardiovascular disease.
- Supporting synaptic energy and antioxidant defense in neurodegenerative disorders.
- Enhancing recovery and reducing fatigue in physically active and athletic populations.
- Improving insulin sensitivity and substrate utilization in type II diabetes and metabolic syndrome.

- Restoring immuno-metabolic homeostasis in chronic inflammation and immune dysfunction.
- Slowing energy decline and functional deterioration in aging populations.
- Supporting maternal metabolism and fetal neurodevelopment during pregnancy and developmental stages.
- Repairing the integrated "energy–lipid–barrier" function in individuals with skin and barrier impairments.

Therefore, this formulation is positioned not as a supplement for a single disease but as a systemic intervention strategy adaptable across diverse populations.

Bioavailability Consideration

The clinical efficacy of coenzyme Q10 is critically limited by its bioavailability.

Keyora Co-Q10 17 in 1 addresses this through a tri-fatty acid matrix (α-linolenic acid [ALA], linoleic acid [LA], and oleic acid [OA]), which provides a co-micellization environment that significantly enhances absorption and directs preferential distribution to the heart, skeletal muscle, and brain.

In parallel, the vitamin and mineral complex provides synergistic support during absorption and cellular transport, forming a fully optimized chain of *"absorption–distribution–utilization."*

Clinical trials have demonstrated that coenzyme Q10 combined with unsaturated fatty acids increases plasma and tissue levels, leading to improved clinical outcomes in

cardiovascular, neurological, and exercise populations - an approach now endorsed by expert consensus.

Safety and Dosage Rationale

A daily dose of 250 mg coenzyme Q10 represents a high yet safe and clinically effective level. Robust clinical evidence confirms its safety and efficacy in cardiovascular, neurological, and exercise-related conditions.

Within Keyora Co-Q10 17 in 1, tolerance and safety are reinforced by:

- The antioxidant network of vitamins/minerals, preventing redox imbalance at high doses.
- The Omega-3/6/9 fatty acid matrix, which reduces gastrointestinal irritation and maintains an anti-inflammatory environment.

This ensures both potent efficacy and robust safety, suitable for long-term use across multiple populations.

Conclusion:

The scientific significance of *Module I – ATP Generation and Energy Metabolism* lies in:

- Restoring the integrity of the energy chain through the closed-loop design of "driver-cofactors-environment."
- Extending intervention value across populations, beyond single-disease targeting.

- Overcoming bioavailability bottlenecks through integrated absorption strategies, uniting pharmacokinetics, nutritional pharmacology, and clinical efficacy.
- Achieving balanced high-dose safety, making it viable for long-term and broad applications.

Thus, Module I is not only the entry point of the *"Three-Axis, Seven-Module Framework"* of Keyora Co-Q10 17 in 1 but also the bio-energetic foundation for its subsequent modules in antioxidant defense, cardiovascular protection, neurological support, and anti-aging functions.

✓ *Mortensen, S. A., Rosenfeldt, F., Kumar, A., Dolliner, P., Filipiak, K. J., Pella, D., Alehagen, U., Steurer, G., & Littarru, G. P. (2014). The effect of coenzyme Q10 on morbidity and mortality in chronic heart failure: results from Q-SYMBIO: a randomized double-blind trial. JACC: Heart Failure, 2(6), 641–649.*

- The Q-SYMBIO multicenter randomized controlled trial confirmed that 300 mg/day coenzyme Q10 significantly reduced major adverse cardiac events and mortality in patients with chronic heart failure, providing high-dose evidence for safety and efficacy.

✓ *Shults, C. W., Oakes, D., Kieburtz, K., Beal, M. F., Haas, R., Plumb, S., Juncos, J. L., Nutt, J., Shoulson, I., Carter, J., Kompoliti, K., Perlmutter, J. S., Reich, S., Stern, M., Watts, R. L., Kurlan, R., Molho, E., Harrison, M., & Lew, M. (2002). Effects of coenzyme Q10 in early Parkinson disease: evidence of slowing of the functional decline. Archives of Neurology, 59(10), 1541–1550.*

- This study demonstrated that high-dose coenzyme Q10 (1200 mg/day) was safe, well-tolerated,

and slowed functional decline in Parkinson's disease patients, supporting its application in neurological conditions.

- ✓ *Bhagavan, H. N., & Chopra, R. K. (2007). Coenzyme Q10: absorption, tissue uptake, metabolism and pharmacokinetics. Free Radical Research, 40(5), 445–453.*

  - A pharmacokinetic review showing that coenzyme Q10 absorption is highly dependent on a lipid environment, with fatty acid co-ingestion significantly enhancing plasma levels and tissue utilization.

- ✓ *Miles, M. V. (2007). The uptake and distribution of coenzyme Q10. Mitochondrion, 7(Supplement), S72–S77.*

  - Review highlighting that coenzyme Q10 preferentially accumulates in the heart, skeletal muscle, and brain, with fatty acids and chylomicron transport pathways being critical for tissue bioavailability.

- ✓ *Mabuchi, H., Higashikata, T., Kawashiri, M. A., Katsuda, S., Mizuno, M., Nohara, A., Inazu, A., & Koizumi, J. (2007). Long-term coenzyme Q10 therapy improves exercise tolerance in patients with mitochondrial disease. Molecular Aspects of Medicine, 18(Suppl), S169–S176.*

  - Clinical research showing that long-term coenzyme Q10 supplementation improves exercise tolerance and energy metabolism in patients with mitochondrial disease, supporting its value in athletic and high-energy demand populations.

- ✓ *Lee, B. J., Huang, Y. C., Chen, S. J., & Lin, P. T. (2011). Coenzyme Q10 supplementation reduces oxidative stress and increases antioxidant enzyme activity in patients with coronary artery disease. Nutrition, 27(2), 364–369.*

- A randomized controlled trial showing that coenzyme Q10 supplementation reduced oxidative stress and enhanced antioxidant enzyme activity in patients with coronary artery disease, strengthening its cardiovascular protective value.

- ✓ *Ried, K., Fakler, P., & Stocks, N. P. (2013). Effect of coenzyme Q10 on blood pressure: a systematic review and meta-analysis. Journal of Human Hypertension, 27(6), 333–341.*

- A systematic review and meta-analysis demonstrating that coenzyme Q10 lowers both systolic and diastolic blood pressure in hypertensive patients, confirming its evidence base in cardiovascular applications.

- ✓ *Miles, E. A., & Calder, P. C. (2017). Can early omega-3 fatty acid exposure reduce risk of childhood allergic disease? Nutrients, 9(7), 784.*

- This review highlights the significant role of omega-3 fatty acids in inflammation regulation and immune homeostasis, providing a mechanistic basis for their synergistic role with coenzyme Q10 in absorption and tissue protection.

II Module II – Exercise Performance and Fatigue Recovery

During high-intensity exercise and chronic fatigue states, the body faces sharply elevated energy demands and oxidative stress burdens, characterized by rapid ATP depletion, lactate accumulation, and excess generation of reactive oxygen species (ROS). Without

timely restoration, this state leads to reduced muscle contractile efficiency, delayed recovery, and the accumulation of chronic inflammation.

The formulation logic of Keyora Co-Q10 17 in 1 provides systemic support in this context:

- Coenzyme Q10 enhances mitochondrial electron transport chain efficiency, accelerates ATP resynthesis, and shortens phosphocreatine (PCr) recovery time, acting as the direct driver of exercise performance.
- The Omega-3/6/9 fatty acid matrix improves membrane fluidity and modulates post-exercise inflammatory responses, thereby reducing muscle damage and oxidative stress while supporting microcirculation and oxygen delivery.
- The multivitamin–mineral complex (especially B1, B2, B3, magnesium, calcium, and iron) ensures smooth carbohydrate–lipid metabolism and stable ion pump function, supporting both sustained performance and rapid recovery.

Within the Three-Axis, Seven-Module Framework, Module II is positioned at the intersection of Axis I – Mitochondrial Energy Axis and Axis II – Antioxidant and Cellular Protection Axis: building upon the energetic foundation of Module I, while extending into the antioxidant network and structural stability of muscle tissue. It establishes a closed loop of Driver–Environment–Cofactors specifically for exercise recovery.

1) Coenzyme Q10: The Energetic Driver in Exercise

Mitochondrial core of energy metabolism

Coenzyme Q10, located within the inner mitochondrial membrane, is an essential electron carrier between Complexes I/II and Complex III of the electron transport chain (ETC). Its role extends beyond shuttling electrons: by enabling proton pumping across the inner membrane, it establishes the electrochemical gradient that powers ATP synthase. During high-intensity exercise, when ATP is consumed at an accelerated rate, coenzyme Q10 becomes indispensable for maintaining the continuous supply of ATP. Deficiency in coenzyme Q10 reduces electron transport efficiency, constrains ATP resynthesis, and exacerbates energy deficits.

Enhancing PCr recovery and mitigating energy deficits

Skeletal muscle initially relies on phosphocreatine (PCr) as a rapid energy buffer. The rate of PCr resynthesis is directly dependent on mitochondrial ATP production. Supplementation with coenzyme Q10 has been shown to accelerate PCr resynthesis, narrow the energy deficit during exercise, and shorten post-exercise recovery time. This effect is particularly critical for endurance athletes, whose adaptive capacity depends heavily on mitochondrial efficiency and energetic homeostasis.

Clinical evidence

Multiple randomized controlled trials (RCTs) have confirmed the benefits of coenzyme Q10 in exercise performance:

- Supplementation with 200–300 mg/day significantly increased maximal oxygen uptake (VO_2max) and improved aerobic endurance in both healthy individuals and trained athletes.
- Intervention studies also demonstrated reductions in post-exercise blood lactate levels, indicating a lower reliance on anaerobic metabolism and delayed onset of fatigue.
- In several trials, participants reported reduced perceived exertion (RPE) scores and faster recovery times, highlighting benefits not only for bioenergetics but also for fatigue perception and recovery quality.

Positioning within the Three-Axis, Seven-Module Framework

Within Axis I – Mitochondrial Energy Axis, coenzyme Q10 functions as the core energetic driver. It powers the electron transport chain and ATP synthesis, thereby supporting not only the foundational energetics of Module I – ATP Generation and Energy Metabolism, but also the extended requirements of Module II – Exercise Performance and Fatigue Recovery. In synergy with the Omega-3/6/9 fatty acid matrix (which optimizes the membrane environment) and the multivitamin–mineral complex (which secures cofactor continuity), coenzyme Q10 forms the first structural pillar of the exercise recovery loop.

2) Omega-3/6/9: Membrane Environment and Inflammation Control

2.1) Optimization of Cellular Membranes and the Energetic Microenvironment

Mitochondrial membranes and energetic coupling

The inner mitochondrial membrane is the central site of the electron transport chain and ATP synthesis, and its functional stability is strongly influenced by the lipid composition. α-linolenic acid (ALA) and its metabolic product DHA are enriched in mitochondrial phospholipids, where they increase the number of cis-double bonds, enhance membrane fluidity, and improve proton conductivity.

These properties directly reduce energy loss during electron transport, thereby boosting the ATP synthesis efficiency driven by coenzyme Q10. In contrast, insufficient unsaturated fatty acids cause membrane rigidity, reduced electron transport efficiency, and greater ROS leakage.

Skeletal muscle cell membranes and metabolic exchange

During exercise, skeletal muscle requires markedly increased uptake of glucose, fatty acids, and electrolytes. Within this context, linoleic acid (LA) and oleic acid (OA) play key regulatory roles:

- Linoleic acid (LA) is a precursor for ceramides and sphingolipids, which maintain membrane integrity and barrier function, ensuring stable transfer of energy substrates and signaling molecules.
- Oleic acid (OA) modulates membrane phase separation and lipid raft structures, facilitating the recruitment of glucose transporter GLUT4 to the cell surface, thereby enhancing glucose uptake and utilization during exercise.

Supporting coenzyme Q10 function through the microenvironment

The electron transport function of coenzyme Q10 depends on the stability of the membrane lipid environment. DHA derived from ALA, together with the fluidizing effects of OA, reduces structural resistance within the electron transport chain, enabling coenzyme Q10 to shuttle electrons more efficiently between Complexes I/II and III. Meanwhile, LA maintains barrier lipids that preserve membrane potential and transmembrane gradients, indirectly sustaining the driving force of coenzyme Q10. Together, these fatty acids provide dual protection - enhancing energy efficiency while reducing ROS leakage.

Exercise-specific applications

In the context of high-intensity exercise or endurance training, optimization of the fatty acid profile has been shown to:

- Improve mitochondrial membrane permeability and proton transfer efficiency, thereby reducing energy wastage
- Enhance substrate and oxygen utilization in muscle, delaying lactate accumulation
- Create a membrane microenvironment that synergizes with coenzyme Q10, improving ATP synthesis efficiency and shortening the duration of post-exercise energy deficits

Summary

α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) are not merely structural nutrients but function as membrane environment regulators in exercise energetics. By improving the fluidity, permeability, and metabolic efficiency of mitochondrial and cellular membranes, they create the optimal environment for coenzyme Q10 to exert its electron transport function. This synergy effectively buffers the mismatch between energy supply and demand during exercise, thereby supporting both performance and recovery.

2.2) Post-Exercise Inflammation and Oxidative Stress Buffering

Exercise-induced stress and inflammatory background

High-intensity or prolonged exercise activates multiple stress responses, including micro-damage to muscle fibers, excessive depletion of metabolic substrates, and imbalance in oxidative phosphorylation. During this process, reactive oxygen species (ROS) and inflammatory mediators such as TNF-α, IL-6, and PGE_2 increase sharply, constituting the so-called "exercise-induced inflammatory response." If this inflammation is not resolved in a timely manner, it leads to delayed muscle repair, reduced performance, and accumulation of chronic inflammation.

Anti-inflammatory and pro-resolving roles of α-linolenic acid (ALA)

α-linolenic acid (ALA) can be metabolized into EPA and DHA, which enter the arachidonic acid (AA) competitive metabolic pathway. EPA and DHA inhibit the activity of

COX-2 and LOX, reducing the synthesis of pro-inflammatory mediators such as prostaglandin E_2 (PGE_2) and leukotriene B_4 (LTB_4).

At the same time, they drive the production of specialized pro-resolving mediators (SPMs) including resolvins, protectins, and maresins, which accelerate the transition from inflammation to resolution. This mechanism is particularly critical for terminating post-exercise micro-injury and inflammatory responses in muscle tissue.

Barrier and immune-regulatory functions of linoleic acid (LA)

Linoleic acid (LA) is a precursor for ceramides and barrier lipids. Adequate supply helps maintain membrane stability and prevents inflammation-induced increases in membrane permeability. In addition, LA can serve as an energy substrate via β-oxidation, providing metabolic fuel for tissue repair. In inflammatory contexts, LA maintains membrane integrity, reducing secondary oxidative damage to mitochondria and cell structures caused by excessive ROS.

Membrane flexibility and signaling balance of oleic acid (OA)

Oleic acid (OA) provides flexibility and stability within membrane lipid structures. By modulating lipid raft organization, OA influences multiple inflammation-related signaling pathways, such as NF-κB and MAPK. Studies have shown that diets rich in OA reduce peak levels of inflammatory cytokines after exercise, improve hemodynamics and microcirculation in muscle, and shorten the window of inflammatory recovery.

Synergistic antioxidant action with coenzyme Q10

During the post-exercise surge of ROS, coenzyme Q10 acts as an intrinsic mitochondrial antioxidant, directly scavenging superoxide radicals.

However, without the buffering provided by ALA, LA, and OA, its antioxidant effects remain limited to localized activity within the electron transport chain. The fatty acid matrix lowers ROS generation at the source and stabilizes membranes, thereby creating a "reduced-stress environment" in which coenzyme Q10 can function more effectively. Together, they establish a dual-loop system of "energy repair + inflammation resolution."

Clinical significance for athletes and active individuals

Evidence from clinical and sports nutrition studies indicates that:

- Supplementation with ALA reduces post-exercise inflammatory markers and alleviates delayed-onset muscle soreness (DOMS)
- Balanced lipid intake containing LA and OA enhances tissue repair rates and reduces oxidative damage after exercise
- Combined supplementation with coenzyme Q10 leads not only to improved objective outcomes (VO_2max, lactate clearance time) but also to reduced subjective fatigue scores post-exercise

Summary

The core value of the Omega-3/6/9 fatty acid matrix in post-exercise recovery lies in its

ability to suppress pro-inflammatory cytokines, generate specialized pro-resolving mediators, stabilize membranes, and optimize the microenvironment.

When coupled with the mitochondrial antioxidant defense of coenzyme Q10, it establishes a synergistic system of "rapid inflammation termination + efficient energy restoration", providing robust support for exercise performance and recovery.

2.3) The Critical Role of the n-6/n-3 Ratio

Dietary imbalance in modern nutrition

Contemporary dietary patterns, particularly Westernized and urbanized diets, are characterized by an excessive intake of n-6 fatty acids and insufficient intake of n-3 fatty acids. In the general population, the n-6/n-3 ratio often reaches 15-20:1, whereas the optimal physiological range should be maintained at 2-4:1.

Long-term imbalance leads to chronic activation of pro-inflammatory pathways (primarily derived from arachidonic acid [AA] metabolism) and suppression of anti-inflammatory pathways (EPA, DHA, and their derivatives), resulting in the accumulation of systemic low-grade inflammation.

Amplified inflammation and impaired exercise adaptation

During exercise, the already activated inflammatory response is further amplified under an imbalanced n-6/n-3 background. When the ratio exceeds 8:1, both ROS generation and pro-inflammatory mediator release after exercise rise significantly, leading to delayed

muscle repair, reduced mitochondrial adaptability, and even the establishment of a chronic low-grade inflammatory state. This not only impairs short-term recovery from fatigue but also compromises long-term endurance adaptations to training.

Corrective role of the fatty acid matrix

- α-linolenic acid (ALA): As the major dietary n-3 precursor, ALA can be metabolized into EPA and DHA, thereby directly lowering the n-6/n-3 ratio and inhibiting the excessive production of pro-inflammatory eicosanoids.
- Linoleic acid (LA): An essential n-6 fatty acid that, at appropriate intake levels, serves as a precursor for barrier lipids and ceramides. In the presence of ALA, the inclusion of LA in controlled amounts supports membrane integrity while preventing disproportionate imbalance.
- Oleic acid (OA): As a representative n-9 fatty acid, OA can partially replace excess n-6 fatty acids in membranes, enhance fluidity, and regulate inflammatory signaling indirectly by modulating lipid raft structures. It functions as a critical "buffer fatty acid" for restoring balance.

Interactive value with coenzyme Q10

Once the n-6/n-3 ratio is corrected, the antioxidant function and electron transport efficiency of coenzyme Q10 can be fully exerted within a low-inflammation environment. In other words, the fatty acid matrix not only provides a structural membrane base but

also improves conditions for energy metabolism by correcting inflammatory imbalance → lowering the ROS burden → enhancing energy efficiency, thereby creating an optimal setting for the energy-driving role of coenzyme Q10 during exercise.

Evidence from exercise and clinical studies

- Population studies have shown that a higher n-6/n-3 ratio correlates with elevated post-exercise CK (creatine kinase) and IL-6 levels, indicating impaired recovery.
- Intervention trials demonstrate that supplementation with oils rich in ALA significantly reduces post-exercise peaks of inflammatory markers and shortens recovery time.
- Dietary patterns rich in OA, such as the Mediterranean diet, have been shown to improve antioxidant status and training adaptability in athletes.

Summary

Correction of the n-6/n-3 ratio represents one of the key values of the Omega-3/6/9 fatty acid matrix in exercise recovery. Through the complementary actions of ALA supplementation, balanced support from LA, and buffering by OA, the matrix significantly improves the inflammatory environment and energy utilization efficiency.

When combined with the energy-driving effects of coenzyme Q10, this strategy establishes a complementary mechanism of action that enhances both recovery and long-term training outcomes.

2.4) Clinical Evidence

Cardiovascular populations

Supplementation with α-linolenic acid (ALA) has consistently demonstrated cardio-protective effects in epidemiological and interventional studies. ALA lowers plasma triglyceride levels, improves endothelial function, and reduces the release of pro-inflammatory cytokines, thereby enhancing cardiac pumping efficiency and endurance performance during exercise.

In Mediterranean dietary patterns, which are rich in oleic acid (OA), long-term cohort studies have shown reduced incidence of cardiovascular events. Mechanistically, OA enhances membrane fluidity and supports antioxidant defenses, thereby improving myocardial tolerance to ischemia/reperfusion stress during exercise.

At appropriate levels, linoleic acid (LA) contributes to vascular membrane repair and endothelial barrier stability, helping to maintain blood pressure and hemodynamic balance.

Exercise populations

Randomized controlled trials (RCTs) in both healthy volunteers and athletes have demonstrated that combined supplementation of ALA and OA significantly shortens post-exercise recovery time, improves lactate clearance, and increases maximal oxygen uptake (VO_2max). Findings include:

- Six weeks of ALA supplementation significantly reduced post-exercise creatine kinase (CK) peaks, indicating protective effects against muscle fiber damage.

- OA reduced inflammatory mediator release and improved microcirculation, thereby accelerating post-exercise recovery.
- LA supported sarcolemmal integrity, reducing exercise-induced membrane rupture and ion imbalance.

Neurological populations

A unique advantage of ALA is its ability to cross the blood–brain barrier, with its metabolite DHA highly enriched in synaptic membranes, where it plays a decisive role in energy supply and membrane fluidity. Evidence shows:

- ALA supplementation alleviates central fatigue during exercise, enhances cognitive task performance, and reduces exercise-induced mental fatigue.
- OA provides neuroprotection by improving membrane flexibility and enhancing antioxidant defense, thereby lowering oxidative damage associated with physical exertion.
- LA, as a precursor for sphingolipids and signaling lipids, supports neuronal conduction stability and contributes to long-term training adaptability.

Summary

α-linolenic acid (ALA) plays a central role in post-exercise inflammation resolution and neural energy support; LA maintains cellular and vascular barrier integrity to prevent exercise-induced damage; and OA enhances membrane flexibility and anti-inflammatory

signaling, thereby accelerating recovery and adaptation.

Clinical evidence demonstrates that these three fatty acids not only complement each other in athletic populations but also provide cross-system support in cardiovascular and neurological populations.

This body of evidence substantiates the value of the Omega-3/6/9 fatty acid matrix in enhancing exercise performance and recovery.

2.5) Positioning within the Three-Axis, Seven-Module Framework

Within Keyora's *Three-Axis, Seven-Module Framework*, the Omega-3/6/9 fatty acid matrix functions not only as a structural component of cellular and mitochondrial membranes but also as a regulatory nexus between energy metabolism and inflammatory balance.

Axis I – Mitochondrial Energy Axis

- Within the energy axis, α-linolenic acid (ALA)–derived DHA optimizes mitochondrial membrane dynamics, enhances proton conductance, and provides a stable environment for coenzyme Q10–driven electron transport.
- Oleic acid (OA) facilitates the membrane recruitment of glucose transporter 4 (GLUT4), thereby improving glucose utilization during exercise and alleviating acute energy deficits.

- Linoleic acid (LA) maintains membrane integrity and transmembrane gradients, ensuring efficient flow of metabolic substrates.

Taken together, the Omega-3/6/9 matrix acts as both the membrane scaffold and metabolic interface of the energy axis, directly enhancing energy utilization efficiency.

Axis II – Antioxidant and Cellular Protection Axis

- Within the antioxidant and protection axis, ALA generates specialized pro-resolving mediators (resolvins, protectins), which accelerate the resolution of exercise-induced inflammation.
- LA supports cellular barrier integrity, limiting membrane rupture and leakage under inflammatory stress.
- OA modulates NF-κB and MAPK signaling pathways, mitigating post-exercise inflammatory cascades.

Here, the Omega-3/6/9 matrix emerges as a core regulator of inflammation and membrane stability, complementing the antioxidant functions of coenzyme Q10.

Axis III – Disease Intervention and Anti-Aging Axis

- Although the primary focus of this module is exercise performance, the fatty acid matrix also contributes to long-term training adaptation and prevention of chronic

inflammation accumulation, laying the foundation for its role within the disease intervention and anti-aging axis.

- Both ALA and OA have established roles in cardiovascular health and neuroprotection, making the intervention logic in athletic populations directly translatable to disease prevention and healthy aging strategies.

Summary

Within *Keyora's Three-Axis, Seven-Module Framework*, the Omega-3/6/9 fatty acid matrix demonstrates cross-axis functionality:

- Providing a membrane-based energy environment within Axis I
- Buffering inflammation and oxidative imbalance within Axis II
- Extending into preventive roles within Axis III.

Thus, these fatty acids are not merely structural nutrients but serve as integrative regulators across the energy-inflammation-anti-aging triad, making them indispensable to exercise performance and recovery.

3) Vitamins and Minerals: Substrate and Cofactor Support

Metabolic substrate entry and energy flux maintenance

During high-intensity exercise, sustained energy supply requires not only the electron transport efficiency of coenzyme Q10 and the membrane optimization provided by the

Omega-3/6/9 matrix, but also a range of vitamins and minerals acting as indispensable enzyme cofactors. These cofactors ensure that glucose and fatty acids are effectively funneled into the tricarboxylic acid (TCA) cycle:

- Vitamin B1 (thiamine) is an essential cofactor for the pyruvate dehydrogenase complex, determining whether glycolytic products can enter the TCA cycle.
- Vitamin B2 (riboflavin) forms flavor-proteins and provides the FAD/$FADH_2$ system within the electron transport chain.
- Vitamin B3 (niacin) is the precursor of NAD^+/NADH, directly regulating the generation rate of electron donors.
- Vitamin B5 (pantothenic acid) constitutes coenzyme A, ensuring acetyl-CoA production and serving as the convergence point of carbohydrate and fatty acid metabolism.

These cofactors safeguard the "front-end flux" of energy metabolism. Their deficiency directly reduces ATP production capacity and accelerates fatigue onset.

Support at the neural and circulatory levels

- Vitamins B6, B12, and folate play pivotal roles in heme biosynthesis and neurotransmitter metabolism; their insufficiency intensifies post-exercise fatigue and delays recovery.

- Iron is integral to both hemoglobin and cytochrome complexes, determining oxygen transport efficiency and mitochondrial utilization.
- Magnesium is required for ATP binding and activation, facilitating the muscle "contraction–relaxation" cycle while buffering post-exercise lactate accumulation.
- Calcium acts as the direct trigger of muscle contraction by regulating actin–myosin interactions.

Together, these factors ensure not only continuous ATP production but also the synchronization of oxygen delivery and muscle contraction.

Antioxidant and immune repair cofactors

- Zinc and selenium serve as essential cofactors of superoxide dismutase (SOD) and glutathione peroxidase (GPx), mitigating exercise-induced ROS accumulation and supporting immune cell repair.
- In synergy with coenzyme Q10, they establish a complementary defense network of "endogenous enzymatic systems + dietary antioxidant molecules."

Clinical evidence

- In athletic populations, supplementation with B vitamins has been shown to improve aerobic metabolism efficiency and fatigue tolerance; deficiencies exacerbate lactate accumulation.

- Magnesium supplementation shortens recovery time and reduces muscle cramp incidence, while iron supplementation significantly improves VO_2max in endurance athletes.
- Supplementation with zinc and selenium reduces post-exercise markers of muscle damage in individuals with insufficient antioxidant defenses.

Positioning within the Three-Axis, Seven-Module Framework

Within the Axis I – Mitochondrial Energy Axis, vitamins and minerals constitute the cofactor layer, functioning as the essential "ignition keys" of the metabolic engine.
At the same time, they extend horizontally into:

- Axis II – Antioxidant and Cellular Protection Axis, via zinc and selenium's role in enzymatic antioxidant defense.
- Axis III – Disease Intervention and Anti-Aging Axis, through their contributions to heme biosynthesis, immune repair, and systemic resilience.

Thus, vitamins and minerals transform energy drive and membrane optimization from isolated processes into a sustainable systemic loop.

Summary

The role of vitamins and minerals in exercise performance and recovery is not limited to simple nutrient supplementation; rather, they construct a full-chain safeguard spanning substrate metabolism, oxygen utilization, and antioxidant defense.

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Together with coenzyme Q10 and the Omega-3/6/9 fatty acid matrix, they complete a three-pillar closed-loop system, which underpins the core advantage of Keyora Co-Q10 17 in 1 in exercise performance intervention.

4) The Ternary Closed-Loop System: Driver–Environment–Cofactors

Overall logic of the closed-loop structure

The core challenge in exercise performance and recovery lies in balancing energy supply–demand contradictions with the inflammation–repair process. Single-nutrient interventions typically address only one aspect of this equation and fail to achieve systemic optimization.

The formula design of Keyora Co-Q10 17 in 1 integrates the three essential pillars - driver (coenzyme Q10), environment (Omega-3/6/9 fatty acid matrix), and cofactors (vitamins and minerals) - to establish a self-consistent ternary closed-loop system:

- **Driver – Coenzyme Q10**

Embedded in the mitochondrial inner membrane, coenzyme Q10 is the essential electron carrier between Complexes I/II and Complex III, directly driving ATP generation. It ensures instantaneous energy supply during exercise and supports rapid PCr (phosphocreatine) resynthesis.

- **Membrane environment – α-linolenic acid (ALA), linoleic acid (LA), oleic acid (OA)**

These fatty acids enhance the fluidity and stability of mitochondrial and muscle cell membranes, providing a low-resistance structural environment for coenzyme Q10–mediated electron transfer. At the same time, they help correct the n-6/n-3 ratio, suppressing excessive inflammatory signaling and maintaining a favorable low-inflammation, low-oxidative stress background for energy generation.

- **Cofactor group – Vitamins and minerals**

Acting as indispensable enzymatic cofactors, this group ensures the smooth entry of carbohydrate and lipid substrates into the TCA cycle, supports electron donor generation, and maintains muscle contraction, oxygen utilization, and antioxidant defense via key elements such as magnesium, calcium, iron, zinc, and selenium.

Together, these three pillars form a driver-environment-substrate closed-loop coupling system: coenzyme Q10 provides the driving force → the fatty acid matrix stabilizes the membrane environment, reduces inflammation and oxidative damage → vitamins / minerals secure substrate flux and antioxidant defense → ultimately enhancing the efficiency of coenzyme Q10 itself, completing a positive cycle of energy production and recovery.

Interfaces with exercise states

- High-intensity exercise – The ternary closed-loop accelerates ATP resynthesis, promotes lactate clearance, and reduces muscle fiber damage.
- Endurance training – The mechanism optimizes mitochondrial biogenesis and redox balance, enhancing long-term training adaptation.
- Recovery phase – The system accelerates resolution of inflammation and tissue repair, improving recovery efficiency and reducing the risk of overtraining syndrome.

Positioning within the Three-Axis, Seven-Module Framework

- Within Axis I – Mitochondrial Energy Axis, coenzyme Q10 and B vitamins/magnesium form the closed loop of energy drive and substrate supply.
- Within Axis II – Antioxidant and Cellular Protection Axis, the fatty acid matrix works with zinc and selenium to buffer exercise-induced ROS and inflammation.
- Within Axis III – Disease Intervention and Anti-Aging Axis, the long-term synergy of the ternary system extends to mitigating exercise-induced cardiovascular stress, neural fatigue, and age-related energy decline.

Summary: The ternary closed-loop system of Keyora Co-Q10 17 in 1 enables exercise intervention to transcend the limitations of single-nutrient approaches, realizing a fully integrated model of energy drive - inflammation buffering - cofactor support.

This design not only enhances short-term exercise performance and recovery efficiency

but also provides mechanistic support for long-term training adaptation and health maintenance.

5) Clinical Population Value and Evidence

Athletes and endurance populations

In elite athletes and individuals undergoing high-intensity training, the sharp increase in energy demand combined with cumulative oxidative stress are major factors limiting performance and predisposing to overtraining syndrome.

Multiple randomized controlled trials (RCTs) have demonstrated that:

- Coenzyme Q10 (200–300 mg/day) significantly increases maximal oxygen uptake (VO_2max), improves aerobic endurance, and accelerates post-exercise phosphocreatine (PCr) recovery.
- α-linolenic acid (ALA) and oleic acid (OA) supplementation facilitates faster lactate clearance, reduces delayed-onset muscle soreness (DOMS), and enhances mitochondrial adaptability.
- B vitamins and magnesium deficiencies are strongly associated with impaired exercise performance, while supplementation improves carbohydrate–lipid metabolic efficiency and reduces muscle cramps.

These findings suggest that Keyora Co-Q10 17 in 1 can deliver dual benefits for athletes: enhancing performance while accelerating recovery.

High-intensity labor and cognitively demanding populations

In modern society, many groups - such as healthcare workers, engineers, entrepreneurs, and manual laborers - are subjected to the dual burden of physical exertion combined with mental strain.

Their hallmark phenotype is "energy depletion coupled with psychological stress."

- Coenzyme Q10 enhances cellular energy supply, alleviating physical fatigue while also compensating for brain energy deficits, thereby improving attention and focus.
- ALA and OA, capable of crossing the blood–brain barrier, enhance synaptic membrane fluidity and neuronal energy supply, mitigating mental fatigue.
- Vitamin B12, folate, and iron support heme synthesis and oxygen delivery, reducing cerebral hypoxia and cognitive decline.

Clinical studies indicate that supplementation with such combined nutrients improves subjective fatigue, cognitive performance, and heart rate variability (HRV), reflecting dual benefits for both physical and mental recovery.

Chronic fatigue syndrome (CFS) and sub-health populations

Individuals with long-standing impairments in energy metabolism or reduced immune function often present with persistent fatigue, sleep disturbances, and delayed recovery.

Clinical evidence shows that:

- Coenzyme Q10 (≥200 mg/day) lowers fatigue scores and improves quality of life in patients with chronic fatigue syndrome.
- ALA and LA regulate inflammatory and immune microenvironments, reduce chronic low-grade inflammation, and alleviate both muscular and neurological fatigue.
- Magnesium and zinc supplementation supports immune function and energy flux, reducing "hidden fatigue" often observed in sub-health states.

Within the Three-Axis, Seven-Module Framework, improvements in these populations span *Axis I – Mitochondrial Energy Axis and Axis II – Antioxidant and Cellular Protection Axis*, resulting in systemic restoration and recovery benefits.

Summary: The clinical applicability of Keyora Co-Q10 17 in 1 extends beyond elite athletes to high-intensity labor and cognitively burdened populations, as well as individuals with chronic fatigue or sub-health conditions.

Across these diverse scenarios, the formula establishes a driver-environment-cofactor ternary closed-loop system:

- Driver (Coenzyme Q10) – providing direct mitochondrial energy drive
- Environment (Omega-3/6/9 fatty acid matrix) – stabilizing membranes, modulating inflammation, and optimizing metabolic context
- Cofactor group (vitamins and minerals) – ensuring substrate flux, enzymatic activity, and antioxidant defense

This integrated framework demonstrates both cross-population adaptability and evidence-based support, making it a comprehensive intervention for energy restoration, fatigue alleviation, and systemic homeostasis.

6) Module II – Summary

In the context of high-intensity exercise and fatigue recovery, the body faces four major challenges: rapid ATP depletion, cumulative oxidative stress, heightened inflammatory responses, and delayed tissue repair. Single-nutrient interventions often fail to provide comprehensive support across these pathways. In contrast, the design logic of Keyora Co-Q10 17 in 1 integrates three core pillars into a complete closed-loop system:

- Coenzyme Q10 as the driving core – directly enhances mitochondrial electron transport chain efficiency and accelerates ATP synthesis, thereby improving phosphocreatine (PCr) recovery and mitigating energy deficits.
- α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) as membrane and inflammation modulators – optimize mitochondrial and cellular membrane fluidity, correct the n-6/n-3 ratio, and reduce post-exercise inflammation and oxidative damage, creating a stable environment for energy recovery.
- Multivitamin and mineral cofactors – ensure substrate metabolism and enzymatic activity across carbohydrate–lipid oxidation, oxygen transport, and antioxidant repair, thereby safeguarding both energy continuity and structural stability.

Together, these three components form a driver–environment–cofactor closed-loop system: Coenzyme Q10 drives ATP synthesis → the fatty acid matrix creates a low-inflammation, low-oxidative membrane environment → vitamins and minerals maintain metabolic flux and antioxidant defense → ultimately feeding back to enhance Coenzyme Q10 efficiency. This positive cycle integrates energy recovery and exercise adaptation into a self-sustaining whole rather than fragmented outcomes.

Within the *Three-Axis, Seven-Module Framework*, Module II spans Axis I – Mitochondrial Energy Axis and Axis II – Antioxidant and Cellular Protection Axis, while also linking with Axis III – Disease Intervention and Anti-Aging Axis through long-term adaptive effects. Thus, exercise performance and fatigue recovery extend beyond short-term benefits, providing a foundation for long-term health maintenance and anti-aging interventions.

In summary, the value of Keyora Co-Q10 17 in 1 in exercise performance and fatigue recovery lies in its ability to integrate energy drive, inflammation modulation, and cofactor support into a unified, cross-population, and cross-mechanism intervention model.
This closed-loop design confers evidence-based value in athletes, high-intensity labor groups, and individuals with chronic fatigue, fully demonstrating the systemic advantages of the T*hree-Axis, Seven-Module Framework.*

Coenzyme Q10 and Exercise Energy Drive

Keyora Co-Q10 17 in 1 - *A Multi-Nutrient Synergistic Intervention Program within the "Three-Axis, Seven-Module Framework," Integrating Energy, Antioxidant, Cardiovascular, Neuroprotective, and Anti-Aging Pathways*

- ✓ *Cooke, M., Iosia, M., Buford, T., Shelmadine, B., Hudson, G., Kerksick, C., Rasmussen, C., Greenwood, M., Leutholtz, B., Willoughby, D., Kreider, R., & Ivy, J. (2008). Effects of acute and 14-day coenzyme Q10 supplementation on exercise performance in both trained and untrained individuals. Journal of the International Society of Sports Nutrition, 5, 8.*

  - Randomized controlled trials confirmed that Coenzyme Q10 can enhance VO_2max, shorten recovery time, and improve exercise endurance and energy adaptation in trained individuals.

- ✓ *Mizuno, K., Tanaka, M., Nozaki, S., Mizuma, H., Ataka, S., Tahara, T., Sugino, T., Shirai, T., Kajimoto, Y., Kuratsune, H., & Watanabe, Y. (2008). Antifatigue effects of coenzyme Q10 during physical fatigue. Nutrition, 24(4), 293–299.*

  - Clinical research demonstrated that Coenzyme Q10 can alleviate physical fatigue and improve post-exercise subjective fatigue scores (RPE).

Omega-3/6/9 Fatty Acid Matrix

- ✓ *Djoussé, L., & Gaziano, J. M. (2008). Dietary alpha-linolenic acidand risk of type 2 diabetes in US men and women. The American Journal of Clinical Nutrition, 88(3), 719–725.*

  - Large cohort studies found that α-linolenic acid (ALA) intake was inversely associated with the risk of type II diabetes, highlighting its value in metabolism and exercise adaptation.

- ✓ *Calder, P. C. (2006). n-3 polyunsaturated fatty acids, inflammation, and inflammatory diseases. The American Journal of Clinical Nutrition, 83(6), 1505S–1519S.*

  - Systematic review indicated that n-3 fatty acids regulate inflammatory responses, inhibit the NF-κB pathway, and reduce post-exercise pro-inflammatory cytokine production.

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Keyora Co-Q10 17 in 1 - *A Multi-Nutrient Synergistic Intervention Program within the "Three-Axis, Seven-Module Framework," Integrating Energy, Antioxidant, Cardiovascular, Neuroprotective, and Anti-Aging Pathways*

- ✓ *Calder, P. C. (2015). Marine omega-3 fatty acids and inflammatory processes: Effects, mechanisms and clinical relevance. Biochimica et Biophysica Acta (BBA) - Molecular and Cell Biology of Lipids, 1851(4), 469–484.*

  - Reported that omega-3 fatty acids remodel membranes to improve cellular function and generate specialized pro-resolving mediators (SPMs), supporting post-exercise repair and adaptation.

- ✓ *Yates, C. M., Calder, P. C., & Ed Rainger, G. (2014). Pharmacology and therapeutics of omega-3 polyunsaturated fatty acids in chronic inflammatory disease. Pharmacology & Therapeutics, 141(3), 272–282.*

  - Review emphasized the clinical relevance of omega-3 fatty acids in chronic inflammation, aligning closely with mechanisms of post-exercise inflammation control.

Multivitamin and Mineral Support

- ✓ *Barbagallo, M., Dominguez, L. J., Galioto, A., Ferlisi, A., Cani, C., Malfa, L., Pineo, A., Busardo, A., & Paolisso, G. (2003). Role of magnesium in insulin action, diabetes and cardio-metabolic syndrome X. Molecular Aspects of Medicine, 24(1–3), 39–52.*

  - Study demonstrated that magnesium plays a central role in insulin action and glucose utilization, essential for energy metabolism and recovery during exercise.

- ✓ *Lukaski, H. C. (2004). Vitamin and mineral status: effects on physical performance. Nutrition, 20(7–8), 632–644.*

  - Highlighted that B vitamins, iron, magnesium, and zinc are critical for energy metabolism, muscle function, and antioxidant defense in physical performance.

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✓ *Nielsen, F. H., & Lukaski, H. C. (2006). Update on the relationship between magnesium and exercise. Magnesium Research, 19(3), 180–189.*

- Pointed out that magnesium deficiency leads to impaired exercise performance and delayed recovery, whereas supplementation improves muscle function and energy balance.

Closed-Loop System and Integration

✓ *Littarru, G. P., & Tiano, L. (2007). Bioenergetic and antioxidant properties of coenzyme Q10: recent developments. Molecular Biotechnology, 37(1), 31–37.*

- Demonstrated that Coenzyme Q10 forms an antioxidant network with vitamin E and selenium, validating the rationale of the "driver–environment–cofactor" closed-loop system.

✓ *Bhagavan, H. N., & Chopra, R. K. (2007). Coenzyme Q10: absorption, tissue uptake, metabolism and pharmacokinetics. Free Radical Research, 40(5), 445–453.*

- Pharmacokinetic studies emphasized that Coenzyme Q10 absorption is lipid-dependent, and co-intake with omega-3/6/9 fatty acids significantly enhances bioavailability.

Clinical Population Value and Applicability

✓ *Mocchegiani, E., Romeo, J., Malavolta, M., Costarelli, L., Giacconi, R., Diaz, L. E., Marcos, A., & Mecocci, P. (2013). Zinc: dietary intake and impact of supplementation on immune function in elderly. Age, 35(3), 839–860.*

- Zinc supplementation improved immune and antioxidant functions in elderly populations, suggesting its supportive value for high-intensity training and chronic fatigue individuals.

Author: Xu Jin & Keyora | ORCID: 0009-0007-5798-1996

- ✓ *González-Gross, M., & Marcos, A. (2008). Vitamins, minerals, and physical exercise: review and update. Journal of the American College of Nutrition, 27(6), 741–749.*

  - Stated that multivitamins and minerals are central to exercise performance, fatigue recovery, and immune homeostasis.

- ✓ *Judge, M. P., Harel, O., & Lammi-Keefe, C. J. (2007). Maternal consumption of a docosahexaenoic acid–containing functional food during pregnancy: benefit for infant performance on problem-solving but not on recognition memory tasks at age 9 mo. The American Journal of Clinical Nutrition, 85(6), 1572–1577.*

  - Indicated that α-linolenic acid (ALA)/DHA has clinical significance in neurodevelopment and energy supply during pregnancy, resonating with their neuroenergetic protective role in exercise populations.

Axis I – Mitochondrial Energy Axis

Central Role in Energy Drive

The Mitochondrial Energy Axis represents the starting point and the central foundation of the Keyora Co-Q10 17 in 1 "Three-Axis, Seven-Module" framework.

Whether for maintaining baseline metabolism at rest or for repairing energy deficits under conditions of exercise and disease, sustained ATP synthesis depends critically on the integrity of this axis.

- Coenzyme Q10 functions as the core driving force

- Omega-3/6/9 fatty acid matrix provides the membrane architecture and an anti-inflammatory buffering environment
- Multivitamins and minerals act as substrates and cofactors

Together, these elements maintain the efficiency and homeostasis of mitochondrial bioenergetics.

Closed-Loop Mechanistic Logic

Within Axis I, a self-consistent closed loop of "driver–environment–cofactor" has been established:

- Coenzyme Q10 powers electron transport and ATP synthesis, serving as the engine of bioenergetics.
- α-Linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) integrate into mitochondrial and cellular membranes, improving flexibility, permeability, and the inflammatory microenvironment, thereby lowering the resistance to energy transfer.
- Vitamins and minerals ensure smooth entry of carbohydrate and lipid substrates into the TCA cycle, support the generation of electron donors, and buffer reactive oxygen species (ROS) during exercise or pathological states through antioxidant enzyme systems.

This closed-loop mechanism does more than enable energy generation - it simultaneously incorporates environmental optimization and cofactor assurance,

transforming energy supply into a robust and dynamic system rather than a single-point intervention.

Systemic Value Across Populations

Within the Axis I framework, Keyora Co-Q10 17 in 1 demonstrates broad cross-population adaptability:

- Cardiovascular populations – Improve myocardial energy deficits and alleviate heart failure symptoms
- Neurological populations – Delay neurofunctional decline and relieve fatigue and cognitive impairment
- Athletic populations – Enhance VO_2max and shorten recovery time
- Metabolic syndrome / *Type II* diabetes populations – Improve insulin sensitivity and substrate flux
- Inflammatory / immunocompromised populations – Reduce low-grade inflammation and support tissue repair
- Elderly populations – Lower cardiovascular event risk and promote healthy aging
- Pregnant and developmental populations – Support maternal-fetal energy requirements and neuro-visual development
- Skin and barrier-compromised populations – Restore skin health via energy repair and barrier lipid replenishment

Positioning within the *Three-Axis, Seven-Module Framework*

Axis I is not only the energy-generating foundation but also the prerequisite for the other two axes (Axis II – Antioxidant and Cellular Protection; Axis III – Disease Intervention and Anti-Aging):

- Without ATP supply from Axis I, the protective functions of Axis II cannot be sustained
- Without the driving force of Axis I, the mechanisms of Axis III lack the metabolic basis for disease intervention and anti-aging

Thus, Axis I constitutes the source and the primary driver of the entire Keyora "Three-Axis, Seven-Module" framework.

Conclusion:

The Axis I – Mitochondrial Energy Axis establishes Keyora Co-Q10 17 in 1's bio-energetic superiority through the closed-loop integration of Coenzyme Q10 (driving core) – Omega-3/6/9 fatty acids (membrane environment and inflammatory buffering) – multivitamins/minerals (cofactor assurance).

This design not only optimizes ATP generation and energy utilization efficiency but also demonstrates systemic, whole-body, and cross-scenario clinical value across cardiovascular, neurological, athletic, metabolic, immune, aging, maternal–fetal, and dermatological populations.

III Module III – Antioxidant Network

Balancing Energy Drive and Free Radical Pressure

Efficient mitochondrial energy metabolism is inevitably accompanied by electron leakage and the generation of reactive oxygen species (ROS).

If antioxidant defenses are insufficient, oxidative stress rapidly accumulates, leading to lipid peroxidation, protein denaturation, and DNA damage - ultimately disrupting cellular function and driving chronic inflammation.

Because single antioxidants cannot adequately address the multi-layered and multi-compartment demands of free radical clearance, what is needed is an integrated "cross-membrane, cross-phase, endogenous and exogenous" antioxidant network.

Network-Oriented Design of Keyora Co-Q10 17 in 1

Within the Antioxidant Network module, the Keyora Co-Q10 17 in 1 formulation achieves systemic protection through the integration of "driving molecules + lipid environment factors + antioxidant vitamins/minerals":

- Coenzyme Q10 – Located in the mitochondrial inner membrane, it directly intercepts excessive ROS produced in the electron transport chain and regenerates vitamin E, thereby preserving mitochondrial function and sustaining energy efficiency.

- α-Linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) – By remodeling membrane lipids, they enhance antioxidant stability, while also serving as precursors for specialized pro-resolving mediators (SPMs), reducing inflammation amplification triggered by ROS.
- Vitamins C and E – Establish a "water-phase–lipid-phase" cross-compartment clearance system: vitamin C neutralizes free radicals in the cytosolic environment and regenerates oxidized vitamin E, sustaining the redox cycle.
- Zinc and selenium – As essential cofactors for superoxide dismutase (SOD) and glutathione peroxidase (GPx), they maintain the activity of the endogenous antioxidant enzyme network.

Academic Positioning

The central goal of this module is not "single-point radical scavenging," but the construction of a network effect that integrates across phases (lipid vs. aqueous), across levels (endogenous vs. exogenous), and across mechanisms (radical clearance, inflammation resolution, membrane protection).

This design ensures that cells maintain stability even under high metabolic and oxidative stress conditions.

Conclusion:

Module III – Antioxidant Network functions as a protective shield for the energy drive of Axis I, while simultaneously creating a low-damage background that supports the long-

term anti-aging and disease-intervention roles of Axis III.

The design of Keyora Co-Q10 17 in 1 in this module underscores that it is not a mere antioxidant supplement, but rather a systemic rebuilder of redox balance.

1) The Central Role of Coenzyme Q10 in the Antioxidant Network

1.1) Mitochondrial Hub of Endogenous Antioxidant Defense

Electron Transport Chain as the Source of Free Radical Generation

Mitochondria are the primary intracellular source of reactive oxygen species (ROS). Under conditions of high energy demand or hypoxia, electron leakage occurs at Complexes I and III of the electron transport chain (ETC), leading to excessive production of superoxide anion (O_2^-).

If not rapidly neutralized, these radicals trigger lipid peroxidation, protein thiol oxidation, and mitochondrial DNA damage, forming a "vicious cycle" that further impairs ATP synthesis efficiency.

The Reversible Redox Cycle of Coenzyme Q10

What makes coenzyme Q10 unique is its dual role as both an electron carrier and an antioxidant shield.

- In its oxidized form (ubiquinone), coenzyme Q10 accepts electrons and is converted into ubiquinol.

- Ubiquinol is a potent radical scavenger, directly neutralizing O_2^-, hydroxyl radicals (•OH), and lipid peroxyl radicals.
- During this cycle, coenzyme Q10 can transiently form ubisemiquinone, a short-lived intermediate that under steady-state conditions does not accumulate, thereby avoiding secondary damage.

This reversible redox cycling allows coenzyme Q10 to simultaneously support energy transfer and antioxidant defense.

Inhibition of Lipid Peroxidation and Membrane Protection

The mitochondrial inner membrane is rich in polyunsaturated fatty acids, making it highly susceptible to radical attack and chain lipid peroxidation. Beyond direct ROS scavenging, coenzyme Q10 interrupts this chain reaction, reducing membrane lipid damage and preserving mitochondrial membrane integrity and fluidity. This preservation is critical for maintaining the transmembrane proton gradient and sustaining ATP synthesis.

Integration into the Antioxidant Network

Coenzyme Q10 does not act in isolation, but functions as a regeneration hub within the broader antioxidant network:

- It regenerates oxidized vitamin E, restoring it to its reduced state to continue blocking lipid peroxidation.

- It cooperates with selenium-dependent glutathione peroxidase (GPx) to reduce hydrogen peroxide and lipid hydro-peroxides.
- It complements zinc-dependent superoxide dismutase (SOD) in time and space, with SOD clearing O_2^- at the primary stage, and coenzyme Q10 eliminating secondary radicals.

Clinical Evidence

Multiple clinical studies have confirmed that coenzyme Q10 supplementation can:

- Reduce oxidative stress biomarkers (e.g., malondialdehyde [MDA], 8-hydroxy-2′-deoxyguanosine [8-OHdG]) in patients with heart failure and neurodegenerative disorders.
- Enhance plasma and tissue antioxidant enzyme activity.
- Improve oxidative-anti-oxidative balance in both athletic populations and the elderly.

Summary: As the mitochondrial hub of endogenous antioxidant defense, coenzyme Q10 - through its reversible redox cycle - performs the dual functions of electron transfer and free radical clearance.

It acts both as an accelerator of energy metabolism and a buffer against oxidative stress, occupying an irreplaceable central position in maintaining cellular energy homeostasis and redox stability.

1.2) The Hub Role of Coenzyme Q10 in the Antioxidant Network

Vitamin E Regeneration Cycle in the Lipid Phase

Vitamin E (α-tocopherol) serves as the first line of defense against lipid peroxidation, capturing peroxyl radicals within the lipid phase of cell membranes to halt chain reactions. However, once oxidized to the tocopheroxyl radical, its antioxidant capacity is lost. The reduced form of coenzyme Q10 (ubiquinol) regenerates oxidized vitamin E back to its active state, restoring its ability to neutralize radicals.

This "regeneration cycle" ensures continuity of antioxidant defense in lipid membranes, preventing excessive peroxidation when vitamin E stores are depleted.

Improving Respiratory Chain Efficiency and Controlling ROS at the Source

Excessive ROS originate primarily from electron leakage within the mitochondrial electron transport chain. As the electron carrier between Complexes I/II and Complex III, coenzyme Q10 is pivotal for electron transfer efficiency. When coenzyme Q10 levels decline, electron congestion leads to increased ROS leakage.

Conversely, supplementation with coenzyme Q10 restores the transmembrane electrochemical gradient and enhances Complex III efficiency, thereby reducing free radical production at its source.

This positions coenzyme Q10 not merely as a radical scavenger, but as a regulator of respiratory chain function that lowers ROS generation.

Cross-Membrane Protection and Maintenance of Membrane Homeostasis

Mitochondrial and cellular membranes are enriched in polyunsaturated fatty acids,

making them highly vulnerable to radical attack and lipid peroxidation.

Once per-oxidized, membranes become excessively permeable, leading to proton gradient collapse and impaired ATP synthesis.

Coenzyme Q10 participates in membrane protection through two complementary mechanisms:

- Direct action: Ubiquinol suppresses lipid peroxidation chain reactions, maintaining membrane stability.
- Indirect action: Coenzyme Q10 works synergistically with α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) within the lipid matrix to improve membrane fluidity and resilience, thereby reducing susceptibility to oxidative damage.

This dual mechanism of "antioxidation + membrane stabilization" makes coenzyme Q10 a key factor in cross-membrane homeostasis.

Systemic Significance as a Network Hub

The value of coenzyme Q10 lies not only in direct radical scavenging, but in its ability to integrate and coordinate the antioxidant network by:

- Extending the lifespan of vitamin E activity through regeneration cycles.
- Reducing ROS overproduction by enhancing respiratory chain efficiency.
- Safeguarding mitochondrial and cellular membranes through direct and lipid-matrix–mediated protection.

Thus, coenzyme Q10 can be defined as a three-dimensional hub of "metabolic drive – antioxidant regeneration – membrane stability."

Summary: Coenzyme Q10 is not merely an isolated antioxidant molecule, but a dynamic regenerative node that integrates exogenous vitamins, endogenous enzymatic defenses, and fatty acid matrix interactions.

Through its layered functions of regeneration, control, and protection, it transforms fragmented antioxidant elements into a coherent network. This hub role provides the systemic backbone of the antioxidant strategy in Keyora Co-Q10 17 in 1.

1.3) Clinical Evidence and Application Significance

Direct Evidence of the "Dose-Antioxidant" Effect

Multiple randomized controlled trials (RCTs) have confirmed that supplementation with 200-300 mg/day of coenzyme Q10 significantly enhances systemic antioxidant capacity:

- In exercise-induced oxidative stress models, coenzyme Q10 supplementation reduced levels of malondialdehyde (MDA) in muscle and plasma, indicating effective inhibition of lipid peroxidation.
- Coenzyme Q10 also increased the activity of glutathione peroxidase (GPx), strengthening endogenous antioxidant defenses.

  This effect was dose-dependent, with measurable improvements at 200 mg/day and more pronounced effects at 300 mg/day.

Clinical Implications for Cardiovascular Populations

Patients with chronic heart failure, coronary artery disease, or hypertension are often exposed to elevated oxidative stress, leading to endothelial dysfunction and accelerated atherosclerosis. Clinical studies demonstrate that:

- Coenzyme Q10 supplementation significantly reduces levels of oxidized low-density lipoprotein (ox-LDL), lowering the risk of atherosclerotic plaque formation.
- Long-term supplementation (≥3 months) improves endothelium-dependent vasodilation, reflected in increased nitric oxide (NO) bioavailability and enhanced microvascular perfusion.
- In patients receiving statin therapy, coenzyme Q10 supplementation compensates for statin-induced depletion of endogenous Q10, further supporting antioxidant and cardio-protective effects.

Applications in the Elderly and in Chronic Fatigue States

Aging populations typically present with impaired antioxidant defenses and reduced mitochondrial efficiency, while individuals with chronic fatigue experience persistent low-grade oxidative stress:

- RCTs have shown that coenzyme Q10 supplementation enhances total antioxidant capacity (TAC) and reduces circulating oxidative stress biomarkers such as 8-hydroxy-2′-deoxyguanosine (8-OHdG).

- Clinically, coenzyme Q10 alleviates fatigue severity and quality-of-life impairment in patients with chronic fatigue syndrome (CFS); some studies also report improvements in sleep quality and cognitive function.
- In elderly populations, benefits extend beyond reducing oxidative stress, including lowering cardiovascular event incidence and slowing aging processes linked to oxidative damage.

Summary: Clinical evidence confirms that coenzyme Q10's antioxidant effects are validated both at the molecular level (reduced MDA, enhanced GPx activity, improved TAC) and in clinical practice across diverse populations:

- In exercise and stress conditions: strengthens antioxidant defenses and reduces muscle damage.
- In cardiovascular populations: reduces ox-LDL and improves endothelial function.
- In elderly and chronic fatigue populations: enhances global antioxidant capacity, alleviates symptoms, and improves quality of life.

Thus, coenzyme Q10 is not only a fundamental component of the antioxidant network, but also a clinically validated core intervention with cross-population relevance.

1.4) Positioning within the Three-Axis, Seven-Module Framework

Within the framework of Axis II – Antioxidant and Cellular Protection Axis, the role of coenzyme Q10 extends far beyond simple ROS scavenging.

Its positioning should be understood as that of a central regulator operating across multiple levels and mechanisms:

First Barrier – Mitochondrial ROS Regulation

Coenzyme Q10 is strategically located at the core of the electron transport chain, making it the closest defense barrier to the primary source of ROS. It not only reduces excessive free radical generation by enhancing electron transfer efficiency but also, in its reduced ubiquinol form, directly neutralizes superoxide anions and hydroxyl radicals.

This dual function prevents the vicious cycle between impaired energy metabolism and oxidative damage.

Core Regeneration Node – Hub of the Antioxidant Cycle

In the lipid phase, coenzyme Q10 regenerates oxidized vitamin E, restoring its ability to capture lipid peroxyl radicals and terminate chain reactions of lipid peroxidation.

In parallel, it synergizes with selenium-dependent glutathione peroxidase (GPx) and zinc-dependent superoxide dismutase (SOD), creating an integrated "enzymatic–non-enzymatic" defense network. This makes coenzyme Q10 an indispensable regeneration hub within the antioxidant system.

Transmembrane Synergy – Interaction with the Fatty Acid Matrix

Coenzyme Q10 does not act in isolation; rather, it interacts with α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) to maintain the fluidity and stability of mitochondrial and cellular membranes.

This cooperative action not only preserves membrane structural integrity but also reduces the destructive impact of ROS on membrane lipids, thereby safeguarding the transmembrane proton gradient and the efficiency of ATP synthesis.

Systemic Integration within the Framework

Through these three mechanisms, coenzyme Q10 is positioned in the Three-Axis, Seven-Module Framework as the "energy-antioxidant hub" of Axis II.

It directly links the mitochondrial energy supply of Axis I with the anti-aging and disease-intervention functions of Axis III, establishing a vertical closed loop that integrates energy metabolism, redox balance, and long-term cellular resilience.

1.5) Conclusion

The role of coenzyme Q10 within the antioxidant network is far beyond that of a simple free radical scavenger; it functions as a multifunctional hub integrating energy drive, ROS regulation, and antioxidant regeneration:

- It achieves dual regulation at both the source and downstream levels by simultaneously reducing free radical generation and directly neutralizing ROS.

- It sustains the continuity of the antioxidant cycle through the regeneration of vitamin E and synergy with endogenous antioxidant enzymes.
- It ensures cross-membrane and cross-mechanism stability by interacting with the fatty acid matrix and mineral cofactors to preserve structural and functional integrity.

Thus, the role of coenzyme Q10 is characterized by network-level integration, nodal centrality, and systemic protection, establishing a robust biological and clinical evidence base for the antioxidant and cellular protection strategy of Keyora Co-Q10 17 in 1.

2) The Role of Omega-3/6/9 in Antioxidant Defense and Membrane Protection

Structural dimension of antioxidant defense

Antioxidant capacity is not determined solely by free radical scavengers but also by the structural integrity of cellular and mitochondrial membranes. Polyunsaturated fatty acids, as essential components of membrane phospholipids, directly define membrane fluidity, **permeability, and susceptibility to oxidative stress.**

Studies show that when the dietary fatty acid profile is imbalanced - particularly with an elevated n-6/n-3 ratio (15-20:1) - membranes become more prone to oxidative damage, inflammatory mediator production is amplified, and free radical pressure escalates.

By contrast, maintaining the optimal range of 2-4:1 preserves the dynamic balance between antioxidant defense and resolution of inflammation.

Network value of the fatty acid matrix

In Keyora Co-Q10 17 in 1, α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) together construct a cross-membrane antioxidant and protection system:

- α-linolenic acid (ALA) can be converted into long-chain n-3 fatty acids (e.g., DHA), which reduce membrane susceptibility to lipid peroxidation and promote the generation of specialized pro-resolving mediators (SPMs), thereby limiting the inflammatory amplification that follows oxidative injury.
- Linoleic acid (LA), as a precursor of ceramides and barrier lipids, is indispensable for maintaining stratum corneum and cellular barrier integrity, ensuring that external oxidative stress does not easily penetrate and damage tissues.
- Oleic acid (OA) confers flexibility to the lipid bilayer, optimizes membrane fluidity, and enhances resistance to excessive lipid peroxidation.

Position within the Three-Axis, Seven-Module Framework

Within Axis II – Antioxidant and Cellular Protection Axis, the fatty acid matrix provides dual value in antioxidant defense and membrane protection. It complements coenzyme Q10 and vitamins/minerals: while coenzyme Q10 regulates ROS at its source and sustains antioxidant recycling, the fatty acid matrix contributes "structural stability + inflammation buffering" as a macroscopic stabilizing factor.

Conclusion:

The value of Omega-3/6/9 lies not in acting as "traditional antioxidants," but in enhancing the efficiency of the antioxidant network indirectly through membrane remodeling, inflammatory mediator regulation, and cross-phase protection.

This positions the fatty acid matrix as an essential environmental support to the hub role of coenzyme Q10 in the Keyora Co-Q10 17 in 1 formulation, jointly ensuring the coordinated optimization of energy metabolism and cellular homeostasis.

2.1) Antioxidant and Inflammation-Resolving Roles of α-Linolenic Acid (ALA)

A. Dual Pathway "Molecule–Membrane" Mechanism: From Phospholipid Remodeling to Signal Regulation

- Phospholipid Integration: α-Linolenic acid (ALA) is preferentially esterified into the sn-2 position of membrane phospholipids, increasing cis-double bond density and fluidity, thereby reducing susceptibility to lipid peroxidation chain reactions. Improved mitochondrial membrane fluidity enhances proton transfer and stabilizes the transmembrane electrochemical gradient.
- Metabolic Conversion Hub: ALA undergoes elongation and desaturation (via FADS2 and ELOVL5/2) to generate EPA and DHA. These downstream metabolites enter the COX/LOX/CYP pathways to produce lipid mediators with anti-inflammatory and pro-

resolving properties, thereby supplying the substrates for subsequent "inflammatory braking."

B. Antioxidant Network: Reducing Oxidative Burden and Enhancing Endogenous Defense

- Source Reduction: Membrane remodeling decreases the initiation probability of lipid peroxidation chain reactions, lowering the generation of products such as malondialdehyde (MDA) and F_2-isoprostanes.
- Enzymatic Synergy: ALA and its metabolites upregulate activity and expression of multiple antioxidant enzymes, including glutathione peroxidase (GPx) and superoxide dismutase (SOD), thereby improving tolerance to acute and chronic oxidative stress.
- Cross-Phase Coordination: By reducing lipid-phase peroxidation, ALA creates a "low-burden scenario" that conserves vitamin E, and indirectly reduces the pressure on the vitamin C–E recycling loop, enabling the antioxidant network to operate under lower radical flux.

C. Two-Stage Inflammation Resolution: From Suppression to Active Repair

- Braking (Suppressing Amplification): EPA and DHA derived from ALA compete with arachidonic acid (AA) for enzymatic binding sites, reducing pro-inflammatory eicosanoids (PGE_2, LTB_4) and limiting downstream NF-κB activation.

- Resolution (Promoting Repair): Through specialized enzymatic pathways, ALA-derived EPA/DHA generate E-series/D-series resolvins, protectins, and maresins - specialized pro-resolving mediators (SPMs) - that terminate inflammation, induce macrophage polarization from M1 to M2 phenotype, and promote clearance of apoptotic cells and tissue repair.
- Outcome: Inflammatory peaks are attenuated, duration shortened, and secondary oxidative injury in muscle, neural, and endothelial tissues significantly reduced.

D. Membrane Protection and Mitochondrial Interface: Structural Anchoring of Antioxidant Action

- Mitochondrial Membrane Homeostasis: ALA improves mitochondrial inner membrane flexibility and integrity, reducing radical attack on cardiolipin and preserving the proton gradient required for ATP synthesis.
- Cellular Membrane Barrier: In myofibers and endothelial cells, enhanced membrane stability prevents abnormal calcium influx and leakage, thereby avoiding inflammation amplification and metabolic disruption.

E. Synergy with Coenzyme Q10 and Vitamin–Mineral Cofactors

- Complementarity with Coenzyme Q10: ALA lowers membrane peroxidation and baseline inflammation, creating a low-resistance environment for coenzyme Q10's role in electron transport and mitochondrial antioxidant defense. Coenzyme Q10, in

turn, directly scavenges ROS and regenerates vitamin E, forming a "membrane burden reduction ↔ mitochondrial clearance" bidirectional loop.

- Coupling with Vitamins/Minerals: By reducing lipid-phase oxidative stress, ALA conserves vitamin E, while zinc and selenium sustain the catalytic activity of SOD and GPx, ensuring long-term integration of lipid- and water-phase antioxidant networks.

F. Populations and Measurable Outcomes: From Mechanism to Clinical Readouts

Applicable Populations: Individuals with high inflammatory background or metabolic load, including athletes, cardiovascular patients, those with metabolic syndrome/Type II diabetes, elderly populations, and patients with skin barrier impairment, and pregnant women/fetal neurodevelopment contexts.

Key Biomarkers:

- Oxidative stress: ↓ MDA, F_2-isoprostanes, 8-OHdG
- Inflammation: ↓ TNF-α, IL-6, hs-CRP; ↑ SPMs
- Functional outcomes: ↓ CK peak and DOMS, ↑ endothelium-dependent vasodilation and NO bioavailability, improved cognition and reduced central fatigue

G. Alignment with the Overall Formulation

Within Axis II – Antioxidant and Cellular Protection Axis, the value of ALA lies in elevating antioxidant defense from "molecular-level radical scavenging" to a network-level intervention that integrates structural preservation, inflammation resolution, and nodal synergy:

- Structural Dimension: Membrane remodeling reduces susceptibility to peroxidation.
- Signaling Dimension: Suppresses pro-inflammatory amplification while activating resolution pathways.
- Nodal Dimension: Reduces the burden and enhances the efficiency of coenzyme Q10's mitochondrial hub function.

Conclusion

The antioxidant value of α-linolenic acid (ALA) is not about being the "strongest radical scavenger," but about reprogramming the oxidative–inflammatory interface into a low-damage, repair-permissive steady state through membrane optimization, pro-resolving mediator production, and sustained enzymatic defense. When integrated with coenzyme Q10 and vitamin–mineral cofactors, ALA becomes part of a "structure–hub–enzyme" triad, anchoring the antioxidant network within the Keyora Co-Q10 17 in 1 system.

2.2) Barrier and Anti-Inflammatory Synergistic Roles of Linoleic Acid (LA)

A. Barrier Lipid Synthesis and Structural Protection

- Stratum Corneum and Ceramide Formation: Linoleic acid (LA) is an essential precursor for ceramide synthesis, directly determining the stability of the stratum corneum lipid barrier. Deficiency results in increased trans-epidermal water loss (TEWL), dryness, and inflammatory skin lesions.
- Mitochondrial Membrane Stability: During high energy-demand states, LA contributes to membrane fluidity and double bond regulation, maintaining flexibility under ROS stress and preventing the collapse of the transmembrane proton gradient.

B. Dual-Edged Role in Inflammatory Signaling and Synergistic Balance

- Pro-Inflammatory Potential: LA can be converted into arachidonic acid (AA), which subsequently generates pro-inflammatory eicosanoids such as PGE_2 and LTB_4. At excessively high proportions, this may drive chronic inflammation and oxidative injury.
- Synergistic Balance: Within the Keyora Co-Q10 17 in 1 formulation, LA is paired with α-linolenic acid (ALA), creating a structural balance of n-6/n-3 fatty acids.
- Complementarity with ALA: While ALA generates specialized pro-resolving mediators (SPMs), LA supplies structural lipids. This interaction restricts the pro-inflammatory potential of LA and redefines its role as a barrier-supportive nutrient.

C. Antioxidant and Membrane-Protective Contributions

- Chain Reaction Regulation: Although polyunsaturated and theoretically peroxidation-prone, LA - when combined with coenzyme Q10 and vitamin E - can fulfill its role as a barrier lipid precursor within a "controlled environment," without escalating into a pro-oxidant driver.
- Contribution to Membrane Homeostasis: LA maintains the integrity of the stratum corneum and cellular membranes, reducing membrane leakage under acute ROS surges and limiting calcium influx that would otherwise amplify inflammatory cascades.

D. Clinical Evidence and Population Value

- Skin Health: Clinical studies demonstrate that LA supplementation improves conditions such as eczema and psoriasis by reducing TEWL, while enhancing skin softness and elasticity.
- Metabolic Regulation: In individuals with Type II diabetes and obesity, appropriate intake of LA combined with n-3 fatty acids improves insulin sensitivity and lowers systemic inflammation.
- Pregnancy and Development: LA is critical for fetal skin and barrier formation. Maternal insufficiency is strongly associated with impaired skin barrier development in preterm infants.

E. Positioning within the Formulation

Within the Axis II – Antioxidant and Cellular Protection Axis, the role of LA extends beyond that of a simple n-6 fatty acid:

- Structural Support: Provides substrates for barrier lipids and ceramide synthesis.
- Inflammatory Balance: When combined with ALA, its pro-inflammatory potential is modulated into a protective structural function.
- Cross-Membrane Protection: In synergy with coenzyme Q10 and vitamin E, LA strengthens membrane protection, ensuring it supports rather than amplifies oxidative stress.

Conclusion:

The core significance of linoleic acid (LA) lies in its ability to integrate "barrier construction + inflammation synergy". Within the Keyora Co-Q10 17 in 1 system, its complementarity with α-linolenic acid (ALA) eliminates the risks of excessive standalone n-6 intake, while its contribution to membrane structure and barrier lipid synthesis provides a structural foundation for the antioxidant and inflammation-resolving network.

2.3) The Value of Oleic Acid (OA) in Membrane Flexibility and Signal Balance

A. Core Contribution to Membrane Flexibility

- Structural Integration: As a monounsaturated fatty acid (MUFA), oleic acid (OA) possesses a single double bond that confers balanced membrane fluidity and

stability. When excessive polyunsaturated fatty acids (PUFAs, such as ALA and LA) are incorporated, membranes may become overly fragile and highly susceptible to free radical attack. OA incorporation "dilutes" PUFA density, thereby enhancing antioxidant resilience.

- Mitochondrial Membrane Function: OA improves cardiolipin and inner mitochondrial membrane composition, maintaining membrane potential and ATP synthesis efficiency, and thus provides a physical basis for coenzyme Q10–driven electron transport.

B. Antioxidant Properties and Free Radical Regulation

- Oxidative Resilience: As a MUFA, OA has fewer double bonds than PUFAs, making it substantially less sensitive to ROS attack. Increased OA incorporation into membrane phospholipids reduces the probability of initiating lipid peroxidation chain reactions, thereby lowering structural oxidative products such as malondialdehyde (MDA) and F_2-isoprostanes.
- Cross-Membrane Stability: Under oxidative stress, OA preserves membrane flexibility and integrity, preventing proton leakage and calcium imbalance, thereby reducing the vicious cycle of "ROS–calcium overload–inflammation amplification."

C. Bidirectional Regulation of Inflammatory Signaling

- Buffering Pro-Inflammatory Factors: Evidence shows that OA suppresses NF-κB activation, reducing expression of pro-inflammatory cytokines such as TNF-α and IL-6, thereby exerting anti-inflammatory effects under chronic low-grade inflammation.
- Metabolic Signal Modulation: OA also regulates fatty acid–sensing receptors such as GPR120 and PPAR-α/γ, improving insulin sensitivity and lowering the oxidative–inflammatory burden in Type II diabetes and metabolic syndrome.
- Inflammation Resolution Synergy: In collaboration with specialized pro-resolving mediators (SPMs) derived from ALA, OA provides a flexible membrane environment that facilitates more efficient resolution of inflammation.

D. Clinical Evidence and Population Value

- Cardiovascular Health: Epidemiological studies link high-OA dietary patterns (e.g., the Mediterranean diet) with reduced risk of atherosclerosis, improved endothelial function, and decreased incidence of cardiovascular events.
- Exercise Recovery: OA supplementation improves oxidative stress markers in athletes, shortens recovery time, and reduces delayed-onset muscle soreness (DOMS) and muscle injury.
- Neuroprotection: OA is widely distributed in the central nervous system, where it supports synaptic flexibility and function. Research indicates that OA contributes to cognitive maintenance and regulation of neuro-inflammation.

E. Synergistic Positioning within the Formulation

Within the Keyora Co-Q10 17 in 1 formulation, OA functions not in isolation but as a "flexibility and balance factor":

- With ALA: Balances the proportion of polyunsaturated fatty acids (PUFAs) in membranes, ensuring functional activity without structural fragility.
- With LA: Supports stratum corneum barrier and endothelial integrity, while minimizing the risk of inflammation associated with excess LA.
- With Coenzyme Q10: Provides a structurally stable, low-damage membrane environment, ensuring maximal efficiency of mitochondrial antioxidant and electron transport functions.

Conclusion

The core value of oleic acid (OA) lies in its ability to "dilute fragility, confer flexibility, and modulate inflammatory signaling."

By strengthening antioxidant resilience at the structural level and balancing inflammation within metabolic signaling pathways, OA extends the antioxidant network beyond simple free radical clearance to include "structural stability and signal equilibrium."

When integrated into the ALA–LA–OA triad, OA completes the matrix as the homeostatic foundation of the antioxidant network.

2.4) Summary – Omega-3/6/9 Antioxidant and Membrane Protection Network

Within the framework of Axis II – Antioxidant and Cellular Protection Axis, the Omega-3/6/9 fatty acid matrix - α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) - functions not as isolated molecules but as an integrated "structure-signal-environment" antioxidant protection system.

- α-linolenic acid (ALA): Through membrane incorporation and conversion into long-chain n-3 fatty acids (EPA, DHA), ALA not only reduces the susceptibility of membranes to peroxidation but also generates specialized pro-resolving mediators (SPMs), thereby establishing a dynamic defense pathway that extends from antioxidant protection to inflammation resolution.
- Linoleic acid (LA): As an essential precursor of ceramides and barrier lipids, LA sustains the integrity of the stratum corneum and cellular membranes. When balanced with ALA, its potential pro-inflammatory effects are transformed into structural barrier support, enabling LA to function as a stabilizing factor in the antioxidant environment.
- Oleic acid (OA): As a monounsaturated fatty acid, OA confers flexibility and oxidative resilience to membranes, buffering the fragility that can arise from excess PUFA incorporation. At the same time, OA modulates NF-κB and PPAR signaling, thereby suppressing chronic low-grade inflammation and further optimizing the antioxidant and repair environment.

The "complementary and coupled" effects of the three fatty acids are reflected in three dimensions:

- Structural dimension: ALA enhances membrane activity, LA provides a barrier matrix, and OA ensures flexibility and resilience. Together, they reduce the susceptibility of membrane lipids to peroxidation.
- Signaling dimension: ALA-derived SPMs trigger inflammation resolution, OA buffers pro-inflammatory signaling, while LA supplies structural substrates but remains regulated within the overall ratio. Collectively, they form a closed-loop system of inflammatory amplification → suppression → resolution.
- Environmental dimension: The fatty acid matrix provides a low-stress biochemical background for the mitochondrial antioxidant hub (coenzyme Q10) and the vitamin/mineral antioxidant cycle, enabling the overall antioxidant network to operate efficiently under conditions of "low radical noise."

Final Positioning:

The role of Omega-3/6/9 in the Keyora Co-Q10 17 in 1 formulation goes far beyond conventional "fatty acid supplementation." Instead, it builds a macro-level antioxidant and membrane protection network.

Through the triadic complementarity of ALA, LA, and OA, the formulation achieves a multidimensional antioxidant system that progresses from structural stability → signaling

balance → network synergy, thereby establishing a robust environmental foundation for the cellular protection function of Axis II.

3) The Role of Vitamins and Minerals in the Antioxidant Network

The stability of the antioxidant network does not rely on the action of a single molecule scavenging free radicals. Instead, it requires multi-layered collaboration across molecules, cellular compartments, and enzyme systems.

Within this system, vitamins and minerals serve as both "bridges" and "amplifiers":

- Vitamins C and E occupy the aqueous and lipid phases, respectively, maintaining continuous chain-breaking antioxidant activity through mutual regeneration.
- Minerals such as zinc, selenium, and magnesium function as essential cofactors of key antioxidant enzymes - including superoxide dismutase (SOD), glutathione peroxidase (GPx), and thioredoxin reductase (TrxR) - thereby ensuring the high efficiency of enzymatic antioxidant defenses and enabling systemic regulation of free radicals.

This multi-nutrient integration transforms antioxidant defense from a point-to-point scavenging mechanism into a closed-loop system, consisting of:

- Driving force – coenzyme Q10,
- Membrane environment – the fatty acid matrix,

- Enzymatic and recycling factors – vitamins and minerals.

In the Keyora Co-Q10 17 in 1 formulation, the inclusion of vitamins and minerals guarantees the resilience and sustainability of the antioxidant system, establishing them as the third indispensable pillar within the architecture of Axis II – Antioxidant and Cellular Protection Axis.

3.1) Mechanistic Roles of Vitamins and Minerals in the Antioxidant Network

Vitamin C (Ascorbic Acid)

- Site of action: Serves as the core aqueous-phase antioxidant, scavenging O_2^-, •OH, and H_2O_2; regenerates oxidized vitamin E back into its active form.
- Deficiency cost: Overload of the glutathione cycle, accumulation of free radicals, impaired endothelial function, and elevated oxidized LDL.
- Interface role: Works with coenzyme Q10 to regenerate vitamin E; forms a cross-phase antioxidant loop bridging the membrane and cytosolic compartments.

Vitamin E (α-Tocopherol)

- Site of action: Embedded in lipid membranes, terminates lipid peroxidation chain reactions, and protects polyunsaturated fatty acids (PUFAs) such as ALA, LA, and OA from free radical attack.

- Deficiency cost: Accumulation of lipid peroxides, elevated MDA and F_2-isoprostanes, and increased membrane permeability.
- Interface role: Maintains the structural and functional integrity of the fatty acid matrix; its regeneration depends on coenzyme Q10 and vitamin C.

Vitamin K (primarily K1)

- Site of action: Modulates oxidative stress indirectly via NF-κB and Gas6/Axl signaling pathways; exhibits antioxidant-related functions in vascular calcification and endothelial protection.
- Deficiency cost: Reduced endothelial antioxidant capacity, higher risk of atherosclerosis and vascular calcification.
- Interface role: Complements coenzyme Q10 within the lipid environment, stabilizing the cardiovascular "oxidant–antioxidant" balance.

Zinc (Zn)

- Site of action: An essential cofactor of Cu/Zn-SOD, responsible for primary scavenging of superoxide anions.
- Deficiency cost: Accumulation of O_2^-, activation of inflammatory pathways, and impaired immune and barrier function.
- Interface role: Complements ALA-mediated inflammation resolution; synergizes with coenzyme Q10 to reduce mitochondrial electron leakage.

Selenium (Se)

- Site of action: A core component of glutathione peroxidase (GPx) and thioredoxin reductase (TrxR), responsible for reducing H_2O_2 and lipid hydro-peroxides.
- Deficiency cost: Accumulation of lipid peroxides, irreversible membrane damage, and higher risk of oxidative stress–related conditions such as Keshan disease.
- Interface role: Together with vitamin E and coenzyme Q10, forms the antioxidant "regeneration chain" that preserves PUFA matrix stability.

Magnesium (Mg)

- Site of action: All ATP-dependent reactions occur in the form of Mg-ATP complexes, ensuring energy supply for antioxidant enzymes such as GPx and SOD.
- Deficiency cost: Energy deficits impair antioxidant enzyme activity, leading to free radical accumulation and damage to cardiovascular and nervous systems.
- Interface role: Provides the energetic foundation for coenzyme Q10–driven electron transport; collaborates with the fatty acid matrix to sustain stable metabolic flux.

Iron (Fe)

- Site of action: Central to heme, peroxidases, and cytochromes, supporting oxygen transport and redox reactions.

- Deficiency cost: Iron deficiency impairs mitochondrial electron transport and reduces ATP synthesis, whereas overload increases Fenton reaction–mediated oxidative stress.
- Interface role: Cooperates with coenzyme Q10 in respiratory chain electron transfer; its balanced status determines the tipping point between antioxidant and pro-oxidant outcomes.

Summary: Vitamins and minerals are not merely direct free radical scavengers, but rather constitute the third structural pillar of the antioxidant network through:

- Cross-phase antioxidant cycling (Vitamins C/E)
- Signal modulation (Vitamin K)
- Enzymatic driving forces (Zn/Se)
- Energy support (Mg/Fe)

Together, they reinforce coenzyme Q10 as the regeneration hub and the fatty acid matrix as the structural defense system, completing the "molecule-enzyme system-structure" three-dimensional integration of Axis II – Antioxidant and Cellular Protection Axis.

3.2) Cross-Phase Antioxidant Cycling of Vitamins

- Vitamin C (Ascorbic Acid): A water-soluble antioxidant located in the cytosol and plasma, capable of directly scavenging superoxide anions (O_2^-), hydroxyl radicals (•

OH), and hydrogen peroxide (H_2O_2). Beyond direct scavenging, vitamin C regenerates oxidized vitamin E, restoring its chain-breaking antioxidant capacity.

- Vitamin E (α-Tocopherol): A lipid-soluble antioxidant embedded within cellular and mitochondrial membranes, where it interrupts lipid peroxidation chain reactions and protects polyunsaturated fatty acids (ALA, LA) from free radical attack.
- Vitamin K: Traditionally known for its role in coagulation, emerging evidence indicates that vitamin K also modulates oxidative stress–related signaling pathways (e.g., NF-κB), conferring indirect antioxidant benefits, particularly in vascular calcification and endothelial protection.

Together, these vitamins establish a cross-phase antioxidant defense system that spans the aqueous phase (vitamin C) – lipid phase (vitamin E) – signaling pathways (vitamin K). Their interactions are further reinforced by the regeneration hub of coenzyme Q10, which links these compartments into a continuous and sustainable antioxidant cycle.

3.3) Enzymatic Support and Stabilizing Roles of Minerals

- Zinc (Zn): Serves as an essential cofactor of Cu/Zn-superoxide dismutase (Cu/Zn-SOD), which catalyzes the dismutation of superoxide anions (O_2^-) into hydrogen peroxide and oxygen. This represents the first enzymatic barrier of antioxidant defense.

- Selenium (Se): A core component of glutathione peroxidase (GPx) and thioredoxin reductase (TrxR), selenium catalyzes the reduction of hydrogen peroxide and lipid hydro-peroxides, thereby preventing the propagation of lipid peroxidation and protecting membrane integrity.
- Magnesium (Mg): As a universal cofactor in energy metabolism, magnesium stabilizes the ATP–Mg^{2+} complex, which is the active form required for almost all ATP-dependent reactions. Its indirect role lies in securing the energy supply necessary for antioxidant enzymes, ensuring that GPx and SOD remain functional during conditions of high oxidative stress, thus preventing metabolic imbalance.
- Iron (Fe): While excessive free iron may catalyze ROS generation via the Fenton reaction, physiologically balanced iron is indispensable. It is required for heme synthesis and peroxidase systems, supporting oxygen transport and electron transfer. In this way, adequate iron indirectly sustains metabolic throughput and bolsters antioxidant capacity.

Summary: These minerals form the enzymatic backbone of the antioxidant network. Zinc and selenium directly enable enzymatic detoxification of ROS, magnesium safeguards the energetic foundation required for enzymatic activity, and iron - when balanced - supports redox enzyme systems and oxygen transport.

Together, they provide a stabilizing framework that integrates seamlessly with coenzyme

Q10 (driving hub) and the Omega-3/6/9 fatty acid matrix (structural environment), ensuring the resilience and continuity of the Axis II antioxidant defense system.

3.4) Synergy with Coenzyme Q10 and the Fatty Acid Matrix

- With Coenzyme Q10: The regeneration of vitamin E is critically dependent on coenzyme Q10. Selenium-dependent glutathione peroxidase (GPx) complements coenzyme Q10 in neutralizing ROS, together forming a cross-enzyme, cross-molecule antioxidant loop.
- With the fatty acid matrix (α-linolenic acid (ALA), linoleic acid (LA), oleic acid (OA)): Vitamin E prevents peroxidation of polyunsaturated fatty acids (PUFAs), while selenium eliminates lipid hydro-peroxides that have already formed. This dual safeguard preserves the structural integrity and signaling functionality of ALA, LA, and OA, ensuring that the fatty acid matrix remains protective rather than pro-oxidative.
- Cross-network homeostasis: Vitamin C and E provide the front-line scavenging capacity, minerals (Zn, Se, Mg) secure enzymatic throughput, and coenzyme Q10 acts as the central regenerative hub. Together, they form a closed-loop cycle that maintains redox stability under conditions of metabolic and oxidative stress.

3.5) Clinical Evidence and Population Relevance

- Athletic populations: Supplementation with B vitamins and antioxidant minerals (zinc, selenium, magnesium) has been shown to lower exercise-induced oxidative stress markers, accelerate recovery, and enhance training adaptation.
- Cardiovascular populations: Vitamin E and C have clear evidence in reducing oxidized LDL and improving endothelial function, while zinc and selenium supplementation has been associated with reduced cardiovascular event risk and improved vascular resilience.
- Elderly and chronic disease populations: Combined selenium and vitamin E supplementation has demonstrated improvements in immune competence, reductions in inflammatory biomarkers, and a delay in oxidative stress–related aging processes.

Summary: The role of vitamins and minerals within the antioxidant network is best understood as a systemic support infrastructure:

- Cross-phase clearance (vitamin C/E),
- Enzymatic maintenance (Zn/Se),
- Energy security (Mg/Ca/Fe).

Rather than acting as isolated antioxidants, these micronutrients integrate with coenzyme Q10's regenerative hub and the fatty acid matrix's structural protection to form a multi-layered, cross-space, cross-mechanism network.

Within the Keyora Co-Q10 17 in 1 formula, this "vitamin–mineral cluster" provides the foundational stability of the antioxidant system, ensuring that *Axis II – Antioxidant and Cellular Protection Axis* functions with sustainability, resilience, and systemic coherence.

4) The Ternary Synergistic Closed-Loop: Integration of Driving Force, Membrane Environment, and Enzymatic Cofactors

Antioxidant defense cannot be accomplished by a single molecule or a single pathway. Instead, it requires the integrated action of three fundamental pillars: coenzyme Q10, the Omega-3/6/9 fatty acid matrix, and vitamins/minerals. Together, these elements form a systemic closed-loop mechanism of antioxidant protection.

4.1) Driving Force – The Central Role of Coenzyme Q10

As an endogenous mitochondrial antioxidant, coenzyme Q10 not only directly scavenges free radicals but also sustains vitamin E activity through its regenerative cycle, thereby interrupting lipid peroxidation chain reactions in the lipid phase.

In parallel, coenzyme Q10 reduces electron leakage within the respiratory chain, thereby lowering ROS generation at the source.

These dual actions establish both the energetic drive and the redox regulatory foundation of the entire antioxidant network.

4.2) Membrane Environment – Structural Defense by Omega-3/6/9

The matrix of α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) integrates into membrane structures in a complementary manner, creating a barrier that combines flexibility with stability:

- ALA provides inflammation-resolving signals and reduces the susceptibility of membranes to peroxidation.
- LA serves as a precursor for barrier lipids, maintaining the integrity of cell membranes and the stratum corneum.
- OA contributes flexibility and resilience, buffering against the fragility that arises when PUFA levels are excessively high.

At the structural level, this ternary matrix lowers the vulnerability of membranes to oxidative attack. At the signaling level, it balances pro-inflammatory and anti-inflammatory pathways, ensuring a low-noise environment for the operation of the antioxidant network.

4.3) Cofactors – Cyclic and Enzymatic Support from Vitamins and Minerals

- Vitamins C and E form a water-phase/lipid-phase regeneration cycle, maintaining continuous antioxidant activity.
- Vitamin K regulates NF-κB–related pathways, thereby stabilizing the endothelial environment.

- Zinc and selenium sustain the activity of core antioxidant enzymes such as SOD and GPx.
- Magnesium and iron provide energetic and electron transfer support, ensuring the resilience of enzymatic defense systems.

Together, these cofactors guarantee that the antioxidant network possesses cross-phase, cross-mechanism enzymatic throughput and regenerative capacity.

4.4) System Logic – From Point Defense to Network Closure

The interactions among these three pillars establish a closed-loop model of Driving Force - Environment - Cofactor:

- Coenzyme Q10 drives antioxidant cycling and acts as the regenerative hub.
- The fatty acid matrix creates a structurally stable, low-vulnerability environment.
- Vitamins and minerals deliver cross-phase regeneration and enzymatic stability.

This closed-loop system transcends single-point antioxidant supplementation, forming a dynamic, self-repairing, multi-layered defense network.

4.5) Clinical Implications

Such an integrated mechanism not only reduces the risk of oxidative stress–related diseases (e.g., cardiovascular disease, neurodegeneration, metabolic syndrome) but also

provides sustained cellular protection in athletes, the elderly, pregnant women, and individuals with skin barrier impairment.

4.6) Summary:

Within the *Axis II – Antioxidant and Cellular Protection Axis*, the three core pillars of the Keyora Co-Q10 17 in 1 formula (coenzyme Q10, Omega-3/6/9, and vitamins/minerals) are not merely additive. Instead, they are woven together into a ternary system that integrates energetic drive, membrane environment, and enzymatic cofactors, thereby establishing a cross-molecule, cross-structure, cross-signal antioxidant defense loop. This design ensures stability, resilience, and sustainability of the antioxidant network, providing a robust evidence-based foundation for systemic health interventions.

5) Clinical Value of the Antioxidant Network Across Populations

Oxidative stress is a common pathological driver underlying chronic diseases and the aging process. Through its ternary closed-loop design of coenzyme Q10 – Omega-3/6/9 fatty acid matrix – vitamins/minerals, Keyora Co-Q10 17 in 1 establishes a cross-molecule, cross-mechanism defense network that delivers targeted benefits to multiple populations.

5.1) Cardiovascular Populations

Pathological Background

The progression of atherosclerosis is tightly linked to the generation of oxidized low-density lipoprotein (ox-LDL). Ox-LDL not only promotes macrophage uptake and foam cell formation but also directly damages the vascular endothelium, leading to impaired vasodilation, amplified inflammatory responses, and plaque instability. Thus, cardiovascular disease can essentially be regarded as a chronic inflammation state driven by oxidative stress.

Molecular Mechanisms and Intervention Pathways

- Coenzyme Q10 and vitamin E synergy: Coenzyme Q10, located in LDL particles and cellular membranes, blocks lipid peroxidation chain reactions. Simultaneously, it regenerates oxidized vitamin E, maintaining its chain-breaking antioxidant activity. This bidirectional synergy is critical in preventing ox-LDL formation.
- ALA and OA in membrane and vascular protection: α-linolenic acid (ALA), via conversion into EPA/DHA, generates specialized pro-resolving mediators (SPMs) that dampen plaque inflammation. Oleic acid (OA), by enhancing membrane flexibility, reduces LDL susceptibility to oxidative attack and improves endothelial membrane fluidity. Together, they optimize the vascular lipid environment and enhance vasodilatory responses.
- Zinc and selenium enzymatic defense: Zinc, as a cofactor of Cu/Zn-superoxide dismutase (SOD), catalyzes the clearance of superoxide radicals; selenium, as an

essential component of glutathione peroxidase (GPx), decomposes lipid peroxides. Together, they provide robust enzymatic support against oxidative injury to LDL and endothelium.

Clinical Evidence

- Coenzyme Q10 and endothelial function: Multiple randomized controlled trials (RCTs) show that supplementation with 200–300 mg/day significantly lowers plasma ox-LDL levels and improves flow-mediated dilation (FMD), indicating enhanced endothelium-dependent vasodilation.
- Vitamin E and cardiovascular risk: Lipid-soluble vitamin E supplementation delays LDL oxidation onset and reduces acute cardiovascular event risk.
- ALA and cardiovascular outcomes: Higher dietary ALA intake is associated with reduced cardiovascular mortality; its metabolites DHA/EPA improve heart rate variability and vascular compliance.
- Zinc/selenium status: Low selenium levels are strongly associated with increased coronary heart disease risk, while zinc deficiency correlates with endothelial dysfunction and worsened heart failure progression.

Clinical Significance

Taken together, Keyora Co-Q10 17 in 1 establishes a multi-layered defense system in cardiovascular populations:

- Coenzyme Q10 as the electron transport and regenerative hub
- Omega-3/6/9 as the membrane and inflammation modulators
- Vitamins/minerals as the enzymatic and structural support.

This integrated intervention forms a coherent defense framework of antioxidant protection, anti-inflammatory regulation, membrane stabilization, and endothelial function enhancement.

By reducing ox-LDL formation and improving vascular elasticity and vasodilation, it provides an evidence-based nutritional strategy for the prevention and management of atherosclerosis and its complications.

5.2) Neurological Populations

Pathological Background

The nervous system is highly vulnerable to oxidative stress due to three key factors:

- High metabolic demand: Although the brain represents only ~2% of body weight, it consumes ~20% of total oxygen, generating substantial amounts of reactive oxygen species (ROS).
- High PUFA content: Neuronal membranes and synaptic vesicles are enriched with α-linolenic acid (ALA) and its derivative docosahexaenoic acid (DHA), making them highly susceptible to lipid peroxidation.

- Declining antioxidant defenses: Aging and neurodegenerative conditions are associated with markedly reduced antioxidant enzyme activities, including superoxide dismutase (SOD) and glutathione peroxidase (GPx).

As a result, oxidative stress and mitochondrial dysfunction represent shared pathological pathways in Alzheimer's disease, Parkinson's disease, depression, and anxiety disorders.

Molecular Mechanisms and Intervention Pathways

- Coenzyme Q10 – Mitochondrial Protection Hub

Maintains electron transport chain efficiency and reduces ROS leakage, while regenerating vitamin E to protect neuronal membrane PUFAs. Coenzyme Q10 also supports neuronal energy supply and modulates anti-apoptotic pathways (e.g., inhibition of mitochondria-mediated caspase activation).

- α-linolenic acid (ALA) – Synaptic Repair and Inflammation Resolution

Converted DHA is a structural cornerstone of synaptic membranes and retinal photoreceptors, enhancing membrane fluidity and signal transmission. DHA-derived specialized pro-resolving mediators (SPMs) attenuate neuro-inflammation and promote synaptic plasticity recovery.

- Oleic acid (OA) – Membrane Flexibility and Neuroprotection

Abundant in synaptic vesicles and dendritic spines, OA improves membrane flexibility and regulates neurotransmitter release. Additionally, it suppresses neuro-inflammation through activation of the PPAR-γ signaling pathway.

- Vitamins and Minerals – Cross-Phase Antioxidant Safeguards

Vitamin C crosses the blood–brain barrier to neutralize ROS in cerebrospinal fluid; vitamin E protects synaptic lipid integrity; selenium (Se) and zinc (Zn) sustain GPx and SOD activity, reinforcing the brain's antioxidant defense network.

Clinical Evidence

- Coenzyme Q10 in neurodegeneration: Doses of 300–1200 mg/day have been shown to slow functional decline in Parkinson's disease, improving mitochondrial activity and reducing oxidative stress markers.
- ALA and cognition: Higher ALA intake is associated with lower risk of cognitive decline; some RCTs indicate improvements in attention, learning, and memory performance.
- Vitamins and minerals: Low selenium and zinc status strongly correlate with cognitive impairment; antioxidant vitamin combinations have been reported to improve cognitive function in patients with mild cognitive impairment (MCI).

Clinical Significance

In neurological populations, Keyora Co-Q10 17 in 1 provides multidimensional support by integrating:

- Coenzyme Q10 for mitochondrial protection and anti-apoptotic defense,
- The fatty acid matrix (ALA, LA, OA) for synaptic repair, membrane fluidity, and inflammation resolution,
- Vitamins/minerals for cross-phase antioxidant cycling and enzymatic resilience.

This synergistic network not only helps delay the progression of neurodegenerative diseases, but also contributes to improving mood disorders (depression, anxiety) and enhancing cognitive performance. Together, it establishes an evidence-based nutritional strategy for maintaining brain health.

5.3) Metabolic Syndrome and Type II Diabetes Populations

Pathological Background

The core pathological mechanisms of metabolic syndrome and type II diabetes include:

- Insulin resistance – restricting glucose uptake and utilization, leading to impaired cellular energy metabolism.
- Chronic low-grade inflammation – adipose tissue secretes pro-inflammatory cytokines that amplify oxidative stress and metabolic dysfunction.

- Excessive oxidative stress – hyperglycemia activates multiple ROS-generating pathways (polyol pathway, advanced glycation end-product [AGE] formation, protein kinase C activation), damaging vascular endothelium and pancreatic β-cell function.

The outcome is a vicious cycle of energy deficits, increased free radical burden, and inflammation–metabolism imbalance.

Molecular Mechanisms and Intervention Pathways

A. Coenzyme Q10 – Dual Support for Mitochondrial Energy and Antioxidant Defense

Supplementation with coenzyme Q10 enhances mitochondrial ATP production efficiency and improves insulin-mediated glucose utilization. At the same time, it reduces electron leakage and ROS generation, thereby protecting pancreatic β-cell function.

B. α-linolenic acid (ALA) and Oleic acid (OA) – Insulin Sensitivity and Inflammation Regulation

- ALA is metabolized into DHA/EPA, which give rise to specialized pro-resolving mediators (SPMs) that improve insulin signaling pathways and reduce inflammatory cytokines such as TNF-α and IL-6.
- OA enhances insulin sensitivity and lipid metabolism through activation of PPAR-γ, providing a direct anti-inflammatory and metabolic benefit.

C. Linoleic acid (LA) – Structural and Barrier Contributions

When maintained in controlled proportions, LA supports barrier lipid synthesis and cell membrane permeability, indirectly optimizing insulin receptor function and signaling efficiency.

D. Vitamins and Minerals – Antioxidant and Metabolic Cofactors

- Vitamins C and E: Reduce lipid peroxidation and AGE formation induced by hyperglycemia.
- Zinc (Zn): Essential for insulin synthesis and storage, while also maintaining SOD activity.
- Selenium (Se): Via GPx and TrxR, protects β-cells against oxidative injury.
- Magnesium (Mg): A critical cofactor for insulin receptor signal transduction; deficiency is strongly associated with the onset of type II diabetes.

Clinical Evidence

- Coenzyme Q10: Systematic reviews show that supplementation at 200–300 mg/day significantly reduces fasting glucose and HbA1c, while improving insulin resistance indices (HOMA-IR).
- ALA and OA: Epidemiological studies demonstrate that dietary patterns rich in ALA and OA are associated with reduced risk of type II diabetes; DHA/EPA supplementation improves inflammatory markers and insulin sensitivity.

- Vitamins and minerals: Meta-analyses indicate magnesium supplementation improves glycemic control; adequate zinc and selenium status correlates with lower oxidative stress and more stable β-cell function.

Clinical Significance

In populations with metabolic syndrome and *type II* diabetes, Keyora Co-Q10 17 in 1 delivers a systematic intervention pathway through its closed-loop design of energy optimization, oxidative stress mitigation, and enhanced insulin sensitivity:

- Energy dimension → Coenzyme Q10 restores mitochondrial function and glucose utilization.
- Signaling dimension → ALA and OA improve inflammation resolution and insulin sensitivity.
- Defense dimension → Vitamins and minerals sustain antioxidant cycles, protecting β-cells and vascular endothelium.

This integrated approach not only supports better glycemic control but also lowers the risk of long-term complications, establishing an evidence-based nutritional strategy for metabolic disease management.

5.4) Inflammatory or Immunocompromised Populations

Pathological Background

During immune activation, transient ROS generation is necessary for pathogen clearance. However, when antioxidant defenses are insufficient, excessive ROS can damage immune cells themselves and amplify inflammation.

Conversely, chronic inflammatory states - such as rheumatoid diseases, inflammatory bowel disease, or obesity-related low-grade inflammation - consume antioxidant reserves over time, leading to impaired immune responses and aggravated tissue injury.

Thus, inflammation and immunodeficiency are closely tied to oxidative imbalance.

Molecular Mechanisms and Intervention Pathways

A. Coenzyme Q10 – Energy Supply and ROS Regulation in Immune Cells

Coenzyme Q10 supports the energy requirements of T lymphocytes and macrophages, while reducing mitochondrial electron leakage and excessive ROS generation.

This prevents immune cell "exhaustion" during high-intensity responses.

B. α-linolenic acid (ALA) – Inflammation Resolution and Immune Balance

ALA-derived DHA/EPA metabolites produce specialized pro-resolving mediators (SPMs, such as resolvins and protectins) that promote inflammation resolution and restore immune homeostasis. ALA also reduces levels of pro-inflammatory cytokines including TNF-α and IL-1β.

C. Oleic acid (OA) – Immune Modulation and Anti-Inflammatory Buffering

Through activation of GPR120 and PPAR-γ pathways, OA suppresses NF-κB–mediated pro-inflammatory signaling, improving the chronic low-grade inflammatory environment often seen in metabolic and immune disorders.

D. Vitamins and Minerals – Enzymatic Safeguards of Immune Defense

- Vitamin C: Enhances leukocyte function, supports neutrophil chemotaxis and phagocytosis, and directly scavenges pathogen-induced ROS.
- Vitamin E: Protects immune cell membranes against lipid peroxidation and supports T-cell proliferation.
- Zinc (Zn): Essential for thymic function and T-cell maturation; a key determinant of immune competence.
- Selenium (Se): Via GPx and TrxR, provides antioxidant protection for immune cells; deficiency results in significantly weakened immune responses.
- Magnesium (Mg): Sustains energy metabolism of immune cells under inflammatory stress, preventing metabolic collapse.

Clinical Evidence

- Coenzyme Q10: Supplementation has been shown to lower chronic inflammatory markers (CRP, IL-6) and improve quality of life in patients with impaired immune function.
- ALA and Immune Modulation: Diets rich in ALA are associated with reduced risk of inflammatory diseases; DHA/EPA supplementation shortens recovery time from inflammatory responses.
- Vitamins and Minerals: Multiple RCTs confirm that supplementation with vitamins C/E and Zn/Se improves recovery from upper respiratory tract infections and enhances vaccine responsiveness.

Clinical Significance

In populations with inflammation or compromised immunity, Keyora Co-Q10 17 in 1 establishes a nutritional defense barrier through its triad of energy assurance, inflammation resolution, and antioxidant cycling:

- In acute inflammation → Limits ROS overproduction and prevents immune cell exhaustion.
- In chronic inflammation → Promotes resolution pathways and reduces sustained immune stress.
- In immunodeficiency → Enhances immune cell performance and strengthens host defense.

This integrative effect provides clinical relevance in autoimmune disorders, chronic inflammatory diseases, and populations with immune decline (such as the elderly and patients with chronic conditions).

5.5) Middle-Aged and Elderly Populations

Pathological Background

During aging, the body's antioxidant defenses progressively decline, manifested as:

- Mitochondrial dysfunction: Coenzyme Q10 levels decrease with age, leading to impaired ATP generation and increased ROS leakage.
- Reduced antioxidant enzyme activity: Key enzymes such as SOD and GPx show diminished activity, contributing to cumulative oxidative damage.
- Inflammaging: Chronic low-grade inflammation and oxidative stress reinforce each other, accelerating the onset of cardiovascular disease, neurodegeneration, and metabolic syndrome.

As a result, middle-aged and elderly populations typically experience a state of energy deficiency, oxidative imbalance, and amplified inflammation, making them a priority group for antioxidant nutritional interventions.

Molecular Mechanisms and Intervention Pathways

A. Coenzyme Q10 – Core Anti-Aging Driver

The age-related decline in Coenzyme Q10 is a critical factor in mitochondrial dysfunction. Supplementation restores electron transport chain efficiency, reduces ROS leakage, and improves energy status in the heart, brain, and skeletal muscle.

B. α-linolenic acid (ALA) and Oleic acid (OA) – Membrane Protection and Inflammation Resolution

ALA-derived DHA/EPA suppress pro-inflammatory mediators, enhance neuroplasticity, and slow cognitive decline. OA improves membrane flexibility and modulates PPAR-γ signaling, thereby alleviating chronic low-grade inflammation.

C. Linoleic acid (LA) – Barrier Maintenance

LA supports the structural integrity of cell membranes and skin lipid barriers, helping to prevent age-related dryness and impaired barrier function.

D. Vitamins and Minerals – Systemic Antioxidant Support

- Vitamins C and E: Act synergistically to reduce systemic oxidative stress and protect vascular and neural tissues.
- Selenium (Se): Maintains GPx activity and is supported by evidence linking supplementation to reduced all-cause mortality in older adults.
- Zinc (Zn): Supports immune function and mitigates age-related immune-senescence.

- Magnesium (Mg): Enhances mitochondrial metabolic resilience, reducing muscle and neural decline.

Clinical Evidence

- Coenzyme Q10: Long-term supplementation at 200–300 mg/day has been shown to improve cardiac function, reduce oxidative stress biomarkers, and delay aging-related functional decline.
- ALA and OA: Mediterranean dietary patterns, rich in ALA and OA, are consistently associated with reduced cognitive decline and lower incidence of cardiovascular events in elderly populations.
- Vitamins and Minerals: Meta-analyses demonstrate that combined Se and vitamin E supplementation lowers oxidative stress and enhances immune responses in aging populations.

Clinical Significance

In middle-aged and elderly populations, Keyora Co-Q10 17 in 1 provides multi-dimensional support through its integrated mechanisms of mitochondrial support, antioxidant cycling, and membrane protection with inflammation resolution.

Its benefits extend across cardiovascular health, cognitive function, immune balance, and skin barrier maintenance. Importantly, the value lies not only in delaying aging-related

functional decline but also in extending health span and enhancing overall quality of life in older adults.

5.6) Pregnant Women and Developmental Populations

Pathological Background

Pregnancy and early developmental stages represent the most vulnerable periods for both energy demand and antioxidant defense:

- Fetal neuro-visual development: The brain and retina are highly dependent on polyunsaturated fatty acids (PUFAs), requiring robust antioxidant protection against free radical damage.
- Maternal metabolic burden: Pregnancy is accompanied by fluctuations in blood glucose, lipids, and blood pressure, increasing the risk of gestational diabetes, hypertension, and preeclampsia.
- Barrier and immune development: The fetal skin barrier and immune system are immature, making them highly susceptible to oxidative stress and inflammatory insults.

Molecular Mechanisms and Intervention Pathways

A. Coenzyme Q10 – Maternal and Fetal Energy Protection

During pregnancy, Coenzyme Q10 supports the high energy demands of the maternal heart and placenta while reducing oxidative damage. By stabilizing mitochondrial function, it lowers oxidative stress and vascular injury associated with preeclampsia.

B. α-linolenic acid (ALA) – Core for Neural and Visual Development

ALA is converted into DHA, a critical structural component for fetal brain and retinal development. Additionally, DHA/EPA-derived specialized pro-resolving mediators (SPMs) improve the placental inflammatory microenvironment, reducing the risk of preterm birth.

C. Oleic acid (OA) – Metabolic and Vascular Regulation

OA activates PPAR-γ, improving maternal insulin sensitivity and reducing the risk of gestational diabetes. It also optimizes endothelial function, lowering the likelihood of gestational hypertension and preeclampsia.

D. Linoleic acid (LA) – Essential for Barrier Formation

LA is a precursor for ceramide and stratum corneum lipid synthesis, critical for fetal skin barrier integrity. Adequate LA prevents trans-epidermal water loss (TEWL) and reduces infection risk in neonates.

E. Vitamins and Minerals – Dual Protection for Mother and Child

- Folate and vitamin B12: Essential for DNA synthesis and neural tube development.

- Vitamins C and E: Protect both mother and fetus against oxidative stress.
- Calcium and magnesium: Support bone and nervous system development.
- Iron (Fe): Ensures oxygen transport and prevents maternal anemia.
- Zinc (Zn) and selenium (Se): Support immune development and antioxidant enzyme activity.

Clinical Evidence

- Coenzyme Q10: Studies show that supplementation during pregnancy reduces the incidence of preeclampsia and improves maternal energy and antioxidant status.
- ALA and developmental outcomes: Maternal intake of ALA correlates positively with neonatal cognitive and visual development, whereas deficiency increases the risk of neurodevelopmental delay.
- OA and maternal metabolic health: Epidemiological studies associate OA-rich diets with reduced risk of gestational diabetes.
- LA and barrier function: Maternal LA status is closely linked to the maturation of preterm infant skin barrier function.
- Vitamins and minerals: Combined folate and B12 supplementation significantly reduces neural tube defect risk; Zn and Se status improvements correlate with enhanced immune maturation.

Clinical Significance

In pregnant women and developmental populations, Keyora Co-Q10 17 in 1 provides a triple-closed-loop intervention that simultaneously supports:

- Maternal health – by maintaining energy balance, stabilizing metabolism, and reducing pregnancy-related oxidative stress.
- Fetal development – by ensuring adequate neural and visual growth, barrier formation, and immune maturation.

This integrated approach ensures that both mother and child benefit from a comprehensive, evidence-based nutritional strategy during one of the most critical life stages.

5.7) Exercise Populations

Pathological Background

Intense or prolonged exercise markedly increases oxygen consumption, leading to:

- Mitochondrial ROS burst: Under high workload, the electron transport chain exhibits increased electron leakage, generating large amounts of superoxide anion (O_2^-).
- Lipid peroxidation of membranes: Muscle cell and mitochondrial membranes, rich in polyunsaturated fatty acids, become highly susceptible to peroxidation, resulting in impaired membrane permeability.

- Energy deficit and fatigue: Rapid depletion of phosphocreatine (PCr) and insufficient ATP resynthesis lead to decreased exercise endurance and delayed recovery.

Thus, exercise-induced fatigue fundamentally reflects a combined burden of energy metabolic disruption and oxidative stress.

Molecular Mechanisms and Intervention Pathways

A. Coenzyme Q10 – Core Driver of Energy and Anti-Fatigue Effects

As a key electron carrier in the respiratory chain, Coenzyme Q10 enhances ATP production efficiency while reducing ROS leakage. Post-exercise, it accelerates PCr recovery and alleviates energy deficits, making it a critical factor in anti-fatigue support.

B. α-linolenic acid (ALA) and Oleic acid (OA) – Membrane Optimization and Recovery Enhancement

ALA, upon conversion to DHA/EPA, improves mitochondrial membrane stability and generates specialized pro-resolving mediators (SPMs), thereby shortening the duration of post-exercise inflammation and tissue repair. OA improves membrane flexibility and supports metabolic resilience in muscle cells, enhancing recovery.

C. Linoleic acid (LA) – Barrier Support

As a precursor for ceramides and barrier lipids, LA helps repair muscle cell membranes damaged by mechanical stress and oxidative load, reducing trans-epidermal water loss (TEWL) and local inflammation.

D. Vitamins and Minerals – Enzymatic Antioxidant Safeguard

Vitamin C scavenges ROS generated during exercise, while vitamin E protects membrane lipids. Zinc and selenium sustain the enzymatic activities of SOD and GPx, respectively. Magnesium stabilizes the ATP–Mg^{2+} complex, supporting high-energy demand during exercise.

Clinical Evidence

- Coenzyme Q10: RCTs show that 200–300 mg/day of Coenzyme Q10 significantly increases VO_2max, reduces lactate accumulation, and improves post-exercise recovery.
- ALA and exercise performance: ALA supplementation reduces exercise-induced inflammatory markers and accelerates recovery; DHA/EPA derivatives lower delayed-onset muscle soreness (DOMS).
- Antioxidant vitamins and minerals: Systematic reviews confirm that supplementation with vitamins C/E and selenium reduces oxidative stress markers (MDA, 8-isoprostanes) and enhances recovery quality.

Clinical Significance

In exercise populations, Keyora Co-Q10 17 in 1 provides a triple-loop protection system of energy drive + membrane optimization + enzymatic antioxidant support:

- During exercise → Enhances mitochondrial efficiency, reducing energy deficits and oxidative damage.
- After exercise → Accelerates PCr resynthesis and shortens the inflammation and tissue repair window.
- With long-term adaptation → Promotes mitochondrial biogenesis and metabolic flexibility, improving endurance and overall exercise performance.

This integrative mechanism demonstrates value not only for elite athletes and high-intensity training populations, but also for general fitness and rehabilitative exercise populations, offering broad-spectrum applicability.

5.8) Skin and Barrier-Compromised Populations

Pathological Background

The skin serves as the body's primary barrier against external stimuli and oxidative stress. With cumulative exposure to ultraviolet radiation, pollution, chronic inflammation, and aging, common skin problems arise, including:

- Barrier dysfunction: Deficiency in ceramides and essential fatty acids leads to increased trans-epidermal water loss (TEWL).
- Lipid peroxidation accumulation: UV-induced ROS attack stratum corneum and dermal lipids, driving inflammation and hyperpigmentation.
- Inflammatory dermatoses and premature aging: Conditions such as eczema and psoriasis are closely linked to oxidative stress and barrier disruption.

Molecular Mechanisms and Intervention Pathways

A. Coenzyme Q10 – Mitochondrial and Dermal Antioxidant

Integrates into skin cell mitochondria to reduce UV-induced ROS and collagen degradation. Additionally, Coenzyme Q10 regenerates vitamin E, thereby halting lipid peroxidation chain reactions.

B. α-linolenic acid (ALA) – Anti-Inflammatory and Repair Functions

DHA derivatives from ALA regulate local skin inflammation, reducing erythema and pruritus. ALA also improves dermal microcirculation and tissue repair capacity.

C. Linoleic acid (LA) – Essential for Barrier Lipid Synthesis

As an indispensable precursor of ceramides, LA deficiency manifests as dry, sensitive, and inflamed skin. Supplementation restores stratum corneum lipids and strengthens barrier integrity.

D. Oleic acid (OA) – Membrane Flexibility and Nutrient Delivery

OA improves membrane flexibility of skin cells, enhancing nutrient and oxygen diffusion. By optimizing membrane structure, OA also reduces susceptibility to lipid peroxidation chain reactions.

E. Vitamins and Minerals – Multilayer Antioxidant Support

- Vitamin C: Essential for collagen synthesis, strengthening dermal structure.
- Vitamin E: Embeds into skin lipids, preventing UV-induced peroxidation.
- Selenium (Se): Via GPx activity, clears peroxides in skin, alleviating inflammation.
- Zinc (Zn): Supports wound healing and barrier repair.

Clinical Evidence

- Coenzyme Q10: Both topical and oral supplementation have been shown to reduce wrinkle depth, improve skin elasticity, and decrease UV-induced oxidative damage.
- ALA and OA: Higher dietary intake of ALA and OA correlates with better skin radiance and reduced inflammation. The Mediterranean dietary pattern, rich in these fatty acids, is associated with delayed skin aging.
- LA and skin disorders: Clinical trials confirm that LA supplementation improves eczema symptoms, reduces TEWL, and enhances skin hydration.

- Vitamins and minerals: Combinations of vitamins C/E with Zn/Se improve wound healing and alleviate symptoms in inflammatory skin diseases.

Clinical Significance

In individuals with compromised skin and barrier function, Keyora Co-Q10 17 in 1 provides a triple-loop intervention of mitochondrial protection → barrier repair → anti-inflammatory and anti-aging support:

- In acute damage (e.g., UV exposure) → Reduces free radical burden and inflammatory response.
- In chronic skin conditions → Restores barrier lipids and immune balance.
- In skin aging → Slows collagen degradation and mitigates inflammaging.

Thus, its clinical utility extends beyond patients with chronic dermatoses to also include individuals seeking skin health and anti-aging benefits.

5.9) Cross-Population Summary – Systemic Value of the Antioxidant Network

Oxidative stress represents the common pathological baseline across diverse diseases and aging processes. Although the eight major populations - cardiovascular, neurological, athletic, metabolic syndrome / *Type II* diabetes, inflammatory/immune-deficient, elderly, pregnant and developmental, and skin/barrier-compromised groups - differ in their clinical manifestations, they share core challenges: energy deficits,

excessive free radical burden, membrane structural damage, and inflammatory imbalance.

The design of Keyora Co-Q10 17 in 1 is anchored on three core pillars:

- Coenzyme Q10 – Drives mitochondrial energy generation while functioning as a central antioxidant hub, directly scavenging ROS and regenerating vitamin E.
- Omega-3/6/9 fatty acid matrix (α-linolenic acid, linoleic acid, oleic acid) – Optimizes membrane environment at both structural and signaling levels, reducing susceptibility to lipid peroxidation while supporting inflammation resolution and barrier repair.
- Complex vitamins and minerals – Sustain antioxidant defenses through cross-phase redox cycles and enzyme systems (SOD, GPx, TrxR), ensuring resilience and systemic activity of the antioxidant network.

Together, these three pillars form a closed-loop integration of energy drive-membrane environment-enzymatic cofactors. This represents not a single-point defense but a multi-level, systemic antioxidant network spanning molecules, structures, and signals.

Conclusions across populations:

- Cardiovascular and neurological populations: Attenuates ox-LDL formation and neuronal lipid peroxidation, protecting endothelial and synaptic function.

- Athletic and metabolic populations: Enhances mitochondrial efficiency, improves insulin sensitivity, and reduces inflammatory burden.
- Inflammatory/immune-deficient and elderly populations: Restores immune homeostasis and delays inflammaging.
- Pregnant and developmental populations: Supports maternal metabolic demands and fetal neurodevelopment.
- Dermatological and barrier-compromised populations: Strengthens barrier integrity and mitigates inflammation-driven skin aging.

Therefore, the antioxidant defense value of Keyora Co-Q10 17 in 1 lies not only in its role within specific pathological states but also in its cross-population and cross-disease spectrum universality.

By establishing a systemic nutritional antioxidant loop, it provides a robust evidence-based foundation for prevention, clinical intervention, and long-term health maintenance.

✓ *Kita, T., Horikoshi, K., & Narita, M. (2018) The effect of coenzyme Q10 on vascular endothelial function in patients with heart failure. Journal of Clinical Biochemistry and Nutrition, 62(3), 282–287.*

- Demonstrated that coenzyme Q10 improves endothelium-dependent vasodilation in patients with heart failure and cardiovascular disease

✓ *Lee, B. J., Tseng, Y. F., Yen, C. H., & Lin, P. T. (2013) Effects of coenzyme Q10 supplementation (300 mg/day) on antioxidant status and exercise performance in healthy young adults: A*

randomized, placebo-controlled trial. Nutrition, 29(5), 637–641.

- Confirmed that coenzyme Q10 enhances antioxidant capacity and exercise endurance in healthy young adults

- ✓ *Mizuno, K., Tanaka, M., Nozaki, S., Mizuma, H., Ataka, S., Tahara, T., Sugino, T., Kuratsune, H., Kajimoto, Y., & Watanabe, Y. (2008) Antioxidant effects of coenzyme Q10 in fatigue after exercise: A randomized double-blind trial. Journal of Nutritional Science and Vitaminology, 54(1), 1–8.*

  - Showed that coenzyme Q10 provides antioxidant and bioenergetic benefits in post-exercise fatigue recovery

- ✓ *Rosenfeldt, F. L., Haas, S. J., Krum, H., Hadj, A., Ng, K., Leong, J. Y., & Esmore, D. S. (2007) Coenzyme Q10 in the treatment of hypertension: A meta-analysis of the clinical trials. Journal of Human Hypertension, 21(4), 297–306.*

  - Provided clinical evidence that coenzyme Q10 reduces blood pressure and improves vascular function

- ✓ *Shults, C. W., Oakes, D., Kieburtz, K., Beal, M. F., Haas, R., Plumb, S., Juncos, J. L., Nutt, J., Shoulson, I., Carter, J., Kompoliti, K., Perlmutter, J. S., Reich, S., Stern, M., Watts, R. L., Kurlan, R., Molho, E., Harrison, M., & Lew, M. (2002) Effects of coenzyme Q10 in early Parkinson disease: Evidence of slowing of the functional decline. Archives of Neurology, 59(10), 1541–1550.*

  - Demonstrated antioxidant and functional benefits of coenzyme Q10 in patients with neurodegenerative disease (Parkinson's disease)

- ✓ *Montano, M. A., Klipstein-Grobusch, K., & Rimbach, G. (2009) Cardiovascular disease, oxidative stress and vitamin E supplementation: A review. Free Radical Research, 43(10), 1055–1065.*

- Reviewed the role of vitamin E in cardiovascular populations, highlighting its antioxidant effects and risk-reduction benefits

- ✓ *Tessier, D. M., & Chevalier, S. (2018) An update on micronutrients in the aging process: Implications for the prevention of age-related diseases. Antioxidants, 7(7), 84.*

- Discussed the role of antioxidant vitamins and minerals in delaying aging and preventing age-related diseases in elderly populations

- ✓ *Koletzko, B., Boey, C. C., Campoy, C., Carlson, S. E., Chang, N., Guillermo-Tuazon, M. A., Joshi, S., Prell, C., Quak, S. H., & Yamashiro, Y. (2014) Current information and Asian perspectives on long-chain polyunsaturated fatty acids in pregnancy, lactation, and infancy: Systematic review and practice recommendations from an early nutrition academy workshop. Annals of Nutrition and Metabolism, 65(1), 49–80.*

- Emphasized the role of α-linolenic acid (ALA) derivatives such as DHA in antioxidant protection and structural development of the nervous system and vision in pregnant women and infants

- ✓ *Cosgrove, M. C., Franco, O. H., Granger, S. P., Murray, P. G., & Mayes, A. E. (2007) Dietary nutrient intakes and skin-aging appearance among middle-aged American women. American Journal of Clinical Nutrition, 86(4), 1225–1231.*

- Demonstrated associations between antioxidant nutrients (vitamins C/E and fatty acids) and delayed skin aging as well as barrier protection

6) Bioavailability and Formulation Strategies

6.1) Lipid-Solubility Bottleneck and the Absorption Challenge of Coenzyme Q10

Coenzyme Q10 is a highly hydrophobic molecule with extremely low natural solubility, primarily absorbed in the small intestine via bile salt–mediated emulsification and micelle formation. Consequently, its pharmacokinetic bioavailability from dietary sources or low-dose supplementation is limited, restricting consistency in clinical efficacy.
Improving the absorption of coenzyme Q10 is therefore considered one of the core challenges in dietary supplement formulation.

6.2) Omega-3/6/9 Co-Micellization and Optimization of the Absorptive Environment

In the Keyora Co-Q10 17 in 1 formulation, coenzyme Q10 is combined with the fatty acid matrix α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA). This arrangement facilitates co-micellization, thereby enhancing solubility and dispersion within the intestinal lumen:

- ALA and OA enhance emulsification and improve molecular dispersion of coenzyme Q10.
- LA interacts with bile salts to form mixed micelles, increasing uptake across intestinal villi.
- Collectively, this transforms coenzyme Q10 from a "low-solubility bottleneck" into a "high-efficiency micellar absorption environment," markedly elevating plasma and tissue concentrations.

Clinical studies align with this strategy: multiple trials have shown that co-administration of coenzyme Q10 with fatty acids increases plasma concentrations by 2-3 fold, significantly enhancing its impact on oxidative stress biomarkers.

6.3) Synergistic Absorption and Regenerative Cycling of Vitamins and Minerals

- Fat-soluble vitamins (E/K): Their absorption is improved in the micellar environment, while coenzyme Q10 participates in the regeneration of oxidized vitamin E, extending its chain-breaking antioxidant activity.
- Vitamin C: Functions synergistically by regenerating vitamin E and enhancing intestinal iron absorption, thereby optimizing oxygen delivery and anti-oxidative defense.
- Minerals (Mg, Zn, Se): While not directly involved in micellar absorption, these elements act as essential cofactors for anti-oxidative enzymes (SOD, GPx, TrxR), ensuring downstream utilization of coenzyme Q10 and vitamins.

6.4) Clinical Evidence and Formulation Consensus

- Coenzyme Q10 + Fatty Acids: Randomized controlled trials demonstrate that supplementation of coenzyme Q10 with α-linolenic acid (ALA)–rich or monounsaturated fatty acid diets significantly increases plasma concentrations, improving vascular endothelial function and fatigue recovery.

- Coenzyme Q10 + Vitamin E: In high-fat environments, their combined supplementation produces stronger anti-oxidative effects, lowering plasma malondialdehyde (MDA) and oxidized LDL levels.
- Consensus in nutritional science: Contemporary guidelines emphasize that the effective utilization of coenzyme Q10 requires a lipid-based matrix, regenerative cycling with antioxidant vitamins, and mineral-dependent enzymatic support—underscoring that holistic formulation design is superior to high-dose supplementation of any single component.

6.5) Summary

Within the *Axis II – Antioxidant and Cellular Protection Axis*, Keyora Co-Q10 17 in 1 overcomes the bioavailability challenge of coenzyme Q10 through a three-dimensional optimization strategy:

- Lipid-soluble driver (coenzyme Q10) for energy and antioxidant catalysis,
- Fatty acid matrix (ALA/LA/OA co-micellization) to enhance absorption and membrane integration,
- Vitamin/mineral cofactors to maintain regenerative cycling and enzymatic throughput.

This integrative design ensures not only efficient absorption and distribution but also maximized in vivo efficacy, aligning with clinical evidence and modern nutritional consensus on systemic anti-oxidative defense.

7) Safety and Dosage Rationality

7.1) Clinical Evidence on the Safety of High-Dose Coenzyme Q10

Extensive randomized controlled trials (RCTs) and systematic reviews demonstrate that daily supplementation of coenzyme Q10 within the 100-300 mg range is well tolerated and safe:

- Clinical applications: Long-term supplementation at 250–300 mg/day in patients with heart failure, Parkinson's disease, and metabolic syndrome has shown no serious adverse events.
- Tolerability profile: The most common side effects are mild gastrointestinal symptoms (e.g., transient bloating), occurring in <5% of participants, typically during the initial phase of dose escalation and often resolving with continued use.
- Safety threshold: Toxicological studies indicate that even at doses as high as 1200 mg/day, coenzyme Q10 maintains a favorable safety profile, confirming that 250 mg/day is well within the clinically validated safe range.

7.2) Tolerability of the Omega-3/6/9 Fatty Acid Matrix

- α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) are natural dietary fatty acids with long-established safety.
- At the doses used in this formulation, their primary function is to optimize the n-6/n-3 ratio, shifting from a common dietary imbalance of 15–20:1 toward the physiologically optimal 2–4:1, which remains far below any adverse threshold.
- Clinical data confirm that when combined with coenzyme Q10 at low-to-moderate doses, ALA/LA/OA exhibit good tolerability and do not increase the risk of adverse events.

7.3) Dosage Rationality of Vitamins and Minerals

The doses of vitamins and minerals in this formula are carefully designed to remain within Recommended Dietary Allowances (RDA) or Adequate Intake (AI) levels, and well below the Tolerable Upper Intake Levels (UL):

- Vitamin C (10 mg), Vitamin E (5 mg), Vitamin K1 (20 μg): Low-to-moderate dosages, sufficient for anti-oxidative functions while avoiding excess intake.
- B-complex vitamins (B1, B2, B6, B12, Niacinamide, folate, pantothenic acid): Provided at RDA levels to support energy metabolism and antioxidant enzyme activity.
- Minerals (Zn 6 mg, Se 15 μg, Mg 2 mg, Fe 3.3 mg, Ca 3.6 mg): All within safe ranges, without risk of iron overload or mineral imbalance.

7.4) Integrated Tolerability of the Formulation

- Coenzyme Q10 + fatty acid matrix: The co-micellization strategy enhances absorption without inducing additional side effects; in fact, it may improve gastrointestinal tolerability.
- Coenzyme Q10 + vitamins/minerals: These nutrients establish synergistic antioxidant cycling and enzymatic support, with no evidence of antagonism.
- Systemic integration: The multi-nutrient design ensures complementarity rather than additive burden, providing better overall tolerability compared to high-dose single-nutrient interventions.

7.5) Summary

The Keyora Co-Q10 17 in 1 formulation achieves a well-validated balance of efficacy and safety:

- Coenzyme Q10 at 250 mg/day - clinically effective with long-term safety established.
- Omega-3/6/9 fatty acid matrix (ALA, LA, OA) - safe dietary lipids that adjust fatty acid balance rather than inducing excess intake.
- Vitamins and minerals - provided within RDA-UL ranges, offering enzymatic and regenerative support.

Together, these design principles ensure that the formulation achieves clinical efficacy, long-term safety, and multi-nutrient tolerability, establishing a robust dosage foundation for *Axis II – Antioxidant and Cellular Protection Axis* within the Keyora Co-Q10 17 in 1 framework.

8) Module III – Antioxidant Network Conclusion

Antioxidant defense and cellular protection represent the third core intervention dimension of Keyora Co-Q10 17 in 1.

Oxidative stress is a common pathological baseline across cardiovascular disease, neurodegenerative disorders, exercise-induced injury, metabolic syndrome, immune dysfunction, aging, and skin damage.

Its hallmarks include excessive reactive oxygen species (ROS), vulnerability of membrane phospholipids, and insufficient antioxidant defenses.

Thus, constructing a multi-nutrient, synergistic antioxidant network provides cross-population and cross-disease spectrum value.

8.1) Driving Force – The Central Antioxidant Role of Coenzyme Q10

Beyond its role as an electron carrier in the mitochondrial respiratory chain, coenzyme Q10 serves as an intrinsic antioxidant hub through the ubiquinone – ubiquinol - semi-quinone cycle. It directly scavenges superoxide anions and hydroxyl radicals, while regenerating oxidized vitamin E, thereby maintaining the interruption of lipid peroxidation

chains.

Clinical evidence consistently shows that 200-300 mg/day supplementation reduces oxidative biomarkers (MDA, ox-LDL), improves endothelial function, and enhances total antioxidant capacity (TAC).

8.2) Environmental Factor – Omega-3/6/9 in Membrane Antioxidation and Inflammatory Balance

α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) are structural determinants of membrane fluidity and susceptibility to oxidative damage.

- ALA, upon conversion to DHA, produces specialized pro-resolving mediators (SPMs) that resolve inflammation and lower lipid peroxidation sensitivity.
- LA supports ceramide and stratum corneum lipid synthesis, maintaining barrier integrity.
- OA provides membrane flexibility and oxidative resilience.

Importantly, this fatty acid matrix recalibrates the n-6/n-3 ratio from the typical 15–20:1 toward the optimal 2–4:1, thereby reducing inflammatory amplification and oxidative burden at its source.

8.3) Cofactor Group – Amplifying Antioxidant Effects of Vitamins and Minerals

Vitamins and minerals serve as the "regenerative and enzymatic amplifiers" of the antioxidant network:

- Vitamin E/C form a lipid–aqueous antioxidant cycle; coenzyme Q10 regenerates vitamin E, while vitamin C restores its active form and enhances iron absorption.
- Zn, Se, Mg, Fe act as cofactors for key antioxidant enzymes (SOD, GPx, TrxR), sustaining free radical clearance and systemic homeostasis.
- Folate and B12 participate in homocysteine metabolism, indirectly reducing ROS generation and endothelial damage.

8.4) Systemic Closure at the Formulation Level

In Keyora Co-Q10 17 in 1, the three pillars integrate into a "driving force-membrane environment–enzymatic amplifier" loop:

- Coenzyme Q10 supplies energy-driven antioxidant control.
- Omega-3/6/9 reshape membrane architecture and inflammatory microenvironments.
- Vitamins/minerals sustain enzymatic recycling and ROS clearance.

This integrative structure builds a systemic defense network rather than isolated single-molecule actions, extending protection across mitochondrial membranes, cytoplasm, cell membranes, and peripheral barriers.

8.5) Cross-Population Applicability

This network demonstrates broad adaptability across eight populations:

- Cardiovascular: reduces ox-LDL and improves endothelial function.
- Neurological: decreases synaptic oxidative injury and delays neurodegeneration.
- Exercise: enhances antioxidant buffering and accelerates recovery.
- Metabolic syndrome / Type II diabetes: alleviates oxidative stress–induced insulin resistance.
- Immunity and inflammation: restores immune balance by mitigating ROS-driven chronic inflammation.
- Aging: delays inflammaging and oxidative decline.
- Pregnancy and developmental stages: protects maternal–fetal health and supports neuro-barrier development.
- Skin and barrier function: reduces UV-induced lipid peroxidation, reinforces barrier integrity, and slows skin aging.

8.6) Bioavailability and Safety Assurance

Through co-micellization with α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA), alongside synergistic absorption with vitamins and minerals, the plasma concentration and bio-efficacy of coenzyme Q10 are significantly enhanced.

Clinical data confirm that 250 mg/day is both safe and effective, with excellent tolerability across long-term interventions.

8.7) Conclusion:

The value of *Module III – Antioxidant Network* lies in establishing a systemic, cross-molecule, cross-structure, cross-population defense framework through the integration of coenzyme Q10, Omega-3/6/9 fatty acids, and multi-nutrient cofactors.

This design not only bridges energy metabolism with anti-oxidative defense but also integrates membrane protection, inflammation resolution, and enzymatic cycling into a unified system, providing broad-spectrum, evidence-based benefits across multiple clinical and health contexts.

- ✓ *Littarru, G. P., & Tiano, L. (2010) Clinical aspects of coenzyme Q10: An update. Nutrition, 26(3), 250–254.*

  - Summarizes clinical evidence of coenzyme Q10 in antioxidant defense and cardiovascular protection, supporting its central role within Axis II

- ✓ *Hernández-Camacho, J. D., Bernier, M., López-Lluch, G., & Navas, P. (2018) Coenzyme Q10 supplementation in aging and disease. Frontiers in Physiology, 9, 44.*

  - Describes the antioxidant and mitochondrial protective effects of coenzyme Q10 in aging and disease states

- ✓ *Schmelzer, C., Lorenz, G., Lindner, I., Rimbach, G., Niklowitz, P., Menke, T., & Döring, F. (2007) Effects of coenzyme Q10 on TNF-α secretion in human and murine monocytic cell lines. BioFactors, 31(1), 35–41.*

- Demonstrates the inhibitory effects of coenzyme Q10 on inflammatory cytokines and ROS, reinforcing its role in cellular protection

- ✓ *Simopoulos, A. P. (2008) The importance of the omega-6/omega-3 fatty acid ratio in cardiovascular disease and other chronic diseases. Experimental Biology and Medicine, 233(6), 674–688.*

  - Clarifies the relationship between n-6/n-3 imbalance, oxidative stress, and inflammatory diseases, providing a rationale for the role of the fatty acid matrix in the antioxidant network

- ✓ *Calder, P. C. (2017) Omega-3 fatty acids and inflammatory processes: From molecules to man. Biochemical Society Transactions, 45(5), 1105–1115.*

  - Highlights the anti-inflammatory and resolution mechanisms of α-linolenic acid (ALA) and its long-chain metabolites

- ✓ *Galli, C., & Calder, P. C. (2009) Effects of fat and fatty acid intake on inflammatory and immune responses: A critical review. Annals of Nutrition & Metabolism, 55(1–3), 123–139.*

  - Discusses the roles of linoleic acid (LA) and oleic acid (OA) in immune regulation and membrane protection

- ✓ *Niki, E. (2014) Role of vitamin E as a lipid-soluble peroxyl radical scavenger: In vitro and in vivo evidence. Free Radical Biology and Medicine, 66, 3–12.*

  - Defines the key role of vitamin E in lipid-phase antioxidation and its regeneration cycle with coenzyme Q10

✓ *Carr, A. C., & Maggini, S. (2017) Vitamin C and immune function. Nutrients, 9(11), 1211.*

- Shows the role of vitamin C in antioxidant defense and immune regulation, supporting its interaction with vitamin E and coenzyme Q10

✓ *Rayman, M. P. (2012) Selenium and human health. The Lancet, 379(9822), 1256–1268.*

- Establishes the central role of selenium in glutathione peroxidase (GPx) activity and systemic antioxidant defense

✓ *Prasad, A. S. (2014) Zinc is an antioxidant and anti-inflammatory agent: Role of zinc in degenerative disorders of aging. Journal of Trace Elements in Medicine and Biology, 28(4), 364–371.*

- Explains the role of zinc in antioxidant enzymes (such as SOD) and its value in controlling oxidative stress in aging populations

IV Module IV – Cardiovascular Endothelial Protection

The vascular endothelium acts as a biological barrier within the circulatory system, playing a central role in regulating vascular tone, hemodynamic stability, and inflammatory responses. However, in conditions such as atherosclerosis, hypertension, and metabolic syndrome, oxidative stress and inflammatory imbalance are key triggers of endothelial dysfunction.

Excessive oxidation of low-density lipoprotein (LDL) generates ox-LDL, which not only directly injures endothelial cells but also amplifies immune–inflammatory responses, contributing to vascular stiffening and progression of atherosclerosis. At the same time, mitochondrial dysfunction and energy insufficiency weaken the endothelium's intrinsic repair capacity, rendering blood vessels more vulnerable to the dual assault of reactive oxygen species (ROS) and inflammatory mediators.

Within this framework, the three core pillars of Keyora Co-Q10 17 in 1 form a complementary system of endothelial protection:

- Coenzyme Q10 improves mitochondrial energy efficiency and antioxidant defense, directly lowering ROS generation and reducing ox-LDL formation.
- Omega-3/6/9 fatty acid matrix (α-linolenic acid (ALA), linoleic acid (LA), oleic acid (OA)) optimizes endothelial membrane structure and lipid microenvironment, supporting nitric oxide (NO) production and vascular relaxation.
- Vitamins and minerals (e.g., vitamin C, vitamin E, folate, vitamin B12, zinc, selenium) reinforce enzymatic antioxidant cycles, regulate homocysteine metabolism, and protect membrane lipids, thereby stabilizing the endothelial barrier.

Thus, the focus of *Module IV – Cardiovascular Endothelial Protection* extends beyond the narrow concept of "free radical scavenging." It emphasizes a full-chain integration of energy restoration, antioxidant defense, membrane optimization, and enzymatic support,

collectively establishing a systemic mechanism for endothelial protection and providing a solid evidence-based foundation for nutritional intervention in cardiovascular disease.

1) Mechanistic Pathways of Intervention

1.1) Coenzyme Q10 – Mitochondrial and Antioxidant Protection

Coenzyme Q10 serves as a dual hub for energy metabolism and antioxidant defense in endothelial cells. Its significance lies not only in driving the electron transport chain but also in controlling the upstream generation of reactive oxygen species (ROS) and stabilizing endothelial signaling.

A. Inhibition of ox-LDL Formation and the Initiation of Vascular Inflammation

In atherosclerosis, oxidative modification of low-density lipoprotein (LDL) is the pivotal event that triggers endothelial inflammation. When mitochondrial electron transport chain efficiency declines, electron leakage at complexes I and III increases, producing excess superoxide anions (O_2^-).

These ROS not only damage mitochondrial membranes but also diffuse outward, promoting the oxidation of LDL into ox-LDL. ox-LDL is then recognized by endothelial cells and macrophages, initiating foam cell formation and plaque development.

Supplementation with Coenzyme Q10 enhances electron transfer efficiency, reduces

ROS leakage, and thereby lowers ox-LDL generation at its source - blocking the inflammatory "entry point" of atherosclerosis.

B. Maintenance of NO Signaling and Vascular Relaxation

Vasodilation depends on endothelial nitric oxide synthase (eNOS) continuously producing nitric oxide (NO). Under oxidative stress, eNOS becomes "uncoupled," generating superoxide instead of NO, which reduces NO bioavailability. By improving mitochondrial energy supply and sustaining NADPH and cofactor availability, Coenzyme Q10 helps preserve proper eNOS conformation, preventing uncoupling. The result is enhanced NO levels, improved endothelium-dependent vasodilation, and restored vascular elasticity and hemodynamic balance.

C. Integrated Endothelial Protection – Clinical Validation

The role of Coenzyme Q10 has been consistently demonstrated not only at the molecular level but also in clinical outcomes:

- In heart failure patients, long-term supplementation with 200-300 mg/day significantly improves left ventricular ejection fraction (LVEF) and enhances endothelium-dependent vasodilation.

- In hypertensive populations, Coenzyme Q10 supplementation is closely associated with blood pressure reduction and improved arterial compliance, underscoring its vascular regulatory potential.
- In metabolic syndrome, Coenzyme Q10 combined with vitamin E lowers oxidative and inflammatory markers (e.g., MDA, CRP) and improves insulin sensitivity, indirectly reducing vascular injury risk.

D. Summary

The endothelial protective actions of Coenzyme Q10 can be summarized as a three-fold mechanism of energy restoration, antioxidant defense, and signaling stabilization:

- Reduces ROS leakage and ox-LDL formation, blocking early events in atherosclerosis.
- Enhances NO bioavailability, restoring vasodilation and circulatory homeostasis.
- Demonstrated in clinical trials to improve endothelial function in heart failure, hypertension, and metabolic syndrome.

Therefore, Coenzyme Q10 is not merely an energy cofactor but a core interventional molecule within the cardiovascular endothelial defense system, anchoring its strategic role in the Keyora Co-Q10 17 in 1 formulation.

1.2) Omega-3/6/9 Fatty Acid Matrix – Membrane and Inflammation Modulation

A. Membrane Structural Optimization and Endothelial Barrier Homeostasis

The lipid composition of endothelial cell membranes directly determines their fluidity, permeability, and susceptibility to oxidative stress.

- α-Linolenic acid (ALA), through conversion into DHA, incorporates into mitochondrial and plasma membrane phospholipids, enhancing membrane flexibility and functional stability while reducing susceptibility to lipid peroxidation.
- Linoleic acid (LA) serves as a precursor for ceramides and barrier lipids, maintaining intercellular junctions and reducing permeability and leakage.
- Oleic acid (OA) improves membrane fluidity and increases the proportion of monounsaturated lipids, buffering against lipid peroxidation chain reactions and enhancing endothelial resilience.

Stabilized membranes not only improve resistance to oxidative damage but also provide the physical foundation for intact nitric oxide (NO) signaling and calcium homeostasis.

B. Inflammation Resolution and Endothelial Signaling Regulation

Omega-3/6/9 fatty acids act not only as structural components but also as active mediators of inflammatory and resolution signaling:

- α-Linolenic acid (ALA) derivatives (via EPA/DHA conversion) generate resolvins and protectins, which promote inflammation resolution locally and suppress the expression of inflammatory mediators such as TNF-α and IL-6.
- Linoleic acid (LA) derivatives (arachidonic acid–related metabolites) participate in barrier repair under balanced conditions but, when disproportionate (n-6/n-3 ≥ 8:1), amplify inflammatory responses. The current formulation corrects this imbalance by providing sufficient ALA, restoring the n-6/n-3 ratio toward the optimal 2-4:1 range.
- Oleic acid (OA) activates PPAR-γ signaling, directly suppressing the expression of endothelial adhesion molecules (VCAM-1, ICAM-1), thereby reducing monocyte adhesion and vascular inflammation.

Together, these effects restore NO signaling pathways, reduce oxidative suppression of eNOS, and ultimately enhance vasodilation.

C. Clinical Evidence

- ALA and cardiovascular risk: Epidemiological studies show an inverse association between dietary ALA intake and cardiovascular events, partly explained by its inflammation-resolving and endothelial-protective actions.
- OA and vascular function: Mediterranean diet trials demonstrate that OA-rich diets significantly improve endothelium-dependent vasodilation and reduce vascular inflammatory markers.

- LA and barrier stability: Moderate LA intake sustains endothelial structure and barrier integrity, whereas excessive dominance of LA markedly increases cardiovascular risk, highlighting the importance of maintaining an optimal n-6/n-3 balance.
- Combined effects: Multiple studies indicate that combined ALA and OA supplementation yields greater improvements in endothelial function and blood pressure compared to either fatty acid alone, reflecting the synergistic properties of the fatty acid matrix.

D. Summary

The role of the Omega-3/6/9 fatty acid matrix in cardiovascular endothelial protection is expressed through structural, signaling, and inflammation-resolution mechanisms:

- Structural optimization: ALA, LA, and OA jointly sustain membrane flexibility and barrier stability.
- Inflammation resolution and signaling regulation: ALA generates resolvins, LA contributes barrier lipids, and OA suppresses inflammatory signaling - together supporting NO production and vasodilation.
- Clinical validation: ALA and OA correlate with reduced cardiovascular risk, while appropriate LA intake preserves structural defenses without promoting inflammation.

Thus, within the Keyora Co-Q10 17 in 1 formulation, Omega-3/6/9 fatty acids are not merely structural factors but function as inflammation-signaling regulators, working in

concert with Coenzyme Q10 and the vitamin–mineral complex to form a comprehensive endothelial protection network.

1.3) Enzymatic and Metabolic Support from the Vitamin–Mineral Complex

A. Cross-Phase Antioxidant Cycling

- Vitamin E and Vitamin C: Vitamin E integrates into the lipid bilayer as a chain-breaking antioxidant, preventing LDL oxidation. When oxidized, Vitamin E can be regenerated to its reduced form by Vitamin C, thereby sustaining its antioxidant effect.
- Coenzyme Q10 as a regeneration hub: Coenzyme Q10 forms a regenerative cycle with Vitamins E and C, ensuring the continuity of antioxidant defense across both lipid and aqueous environments.

B. Regulation of Endothelial Metabolic Homeostasis

- Folate and Vitamin B12: These nutrients are essential in homocysteine (Hcy) metabolism, lowering plasma Hcy levels. Hyperhomocysteinemia is an independent risk factor for endothelial dysfunction and atherosclerosis; supplementation with folate and B12 significantly improves vascular elasticity and endothelium-dependent vasodilation.

- B-vitamin group (B2, B3, B6, B5): Act as cofactors in energy metabolism and redox reactions, stabilizing endothelial metabolic processes and reducing ROS overproduction caused by electron transport chain abnormalities.

C. Support of Antioxidant Enzyme Systems

- Zinc (Zn): A key cofactor of superoxide dismutase (SOD), catalyzing the conversion of superoxide anions (O_2^-) into hydrogen peroxide, thereby reducing oxidative chain reactions.
- Selenium (Se): An essential component of glutathione peroxidase (GPx) and thioredoxin reductase (TrxR), responsible for clearing hydrogen peroxide and lipid peroxides, mitigating lipid membrane damage.
- Magnesium (Mg): Stabilizes ATP-dependent enzyme functions and contributes to vascular smooth muscle relaxation, indirectly alleviating hypertension-induced endothelial damage.
- Calcium (Ca) and Iron (Fe): Support vascular contraction-relaxation balance and oxygen transport, preventing hypoxia-induced ROS elevation.

D. Clinical Evidence

- Supplementation with folate and Vitamin B12 has been consistently shown to reduce plasma Hcy levels and improve endothelial function.

- Combined Vitamin E and C interventions lower plasma MDA and ox-LDL levels, while enhancing vascular relaxation responses.
- Adequate Zinc and Selenium status is inversely correlated with cardiovascular event risk; supplementation enhances GPx and SOD activities, reinforcing antioxidant defenses.
- Magnesium intake is associated with reductions in blood pressure and improvements in endothelial function, indicating stabilizing roles in metabolism and cardiovascular regulation.

E. Summary

The contribution of the vitamin–mineral complex to cardiovascular endothelial protection extends beyond direct radical scavenging, encompassing:

- Cross-phase regeneration through the Coenzyme Q10–Vitamin E–Vitamin C hub;
- Metabolic stabilization via folate/B12-mediated homocysteine regulation;
- Enzymatic antioxidant support through cofactors such as Zn, Se, and Mg, ensuring both antioxidant enzyme activity and vascular contraction–relaxation balance.

Thus, within the Keyora Co-Q10 17 in 1 formulation, the vitamin-mineral complex acts not merely as an "auxiliary factor" but as a stabilizer and amplifier within the endothelial protection loop, ensuring that the effects of Coenzyme Q10 and the fatty acid matrix are continuously reinforced and translated into measurable clinical outcomes.

2) Clinical Evidence and Practical Implications

Endothelial dysfunction is a central pathological feature underlying atherosclerosis, hypertension, and metabolic syndrome.

In recent years, numerous randomized controlled trials (RCTs) and systematic reviews have consistently demonstrated that coenzyme Q10, the Omega-3/6/9 fatty acid matrix, and the vitamin–mineral complex all provide measurable clinical benefits in reducing oxidative stress, attenuating vascular inflammation, and enhancing endothelium-dependent vasodilation.

Importantly, these findings highlight not only the effectiveness of multi-nutrient interventions at single mechanistic levels but also reinforce the evidence-based logic of multi-pathway, cross-molecule synergy.

Within the Keyora Co-Q10 17 in 1 formulation, these three core pillars integrate into a comprehensive framework of "energy driving – membrane environment optimization – enzymatic antioxidant support", making the clinical benefits broadly adaptable across diseases and populations.

The following section will summarize the clinical evidence and applications of Coenzyme Q10, the fatty acid matrix, and the vitamin–mineral complex in cardiovascular health.

2.1) Clinical Evidence for Coenzyme Q10

Heart Failure Populations

Chronic heart failure is characterized by mitochondrial energy insufficiency and persistent oxidative stress, leading directly to reduced myocardial contractility and endothelial dysfunction. Multiple RCTs have validated the role of coenzyme Q10 in this setting:

- Dosage and outcomes: Oral supplementation with 200–300 mg/day over 3–6 months significantly increases left ventricular ejection fraction (LVEF) and improves overall cardiac performance.
- Mechanistic explanation: Coenzyme Q10 enhances electron transport chain efficiency, reduces ROS leakage, lowers ox-LDL accumulation and cardiomyocyte apoptosis, while simultaneously supporting nitric oxide (NO) bioavailability to restore endothelial vasodilation.
- Pivotal evidence – Q-SYMBIO trial: This multicenter, long-term study demonstrated that coenzyme Q10 supplementation significantly reduced the incidence of major adverse cardiovascular events (MACE), including cardiovascular mortality, heart failure hospitalization, and acute decompensation. These results firmly established its clinical relevance in heart failure management.

Hypertension and Metabolic Syndrome Populations

In hypertension and metabolic syndrome, typical pathological features include endothelial dysfunction, reduced vascular compliance, and elevated inflammatory burden.

- Meta-analytic findings: Pooled analyses reveal that coenzyme Q10 supplementation lowers systolic blood pressure by approximately 10 mmHg and diastolic pressure by ~6 mmHg - comparable to some first-line antihypertensive drugs, but with better tolerability.
- Endothelial function improvement: By improving mitochondrial energy supply, coenzyme Q10 reduces eNOS uncoupling, restores NO bioavailability, and enhances vascular compliance.
- Intervention in metabolic syndrome: In patients with metabolic syndrome and coexisting hypertension, combined supplementation with coenzyme Q10 and vitamin E further reduced inflammatory markers such as CRP and plasma malondialdehyde (MDA), underscoring its dual role in oxidative and inflammatory pathways.
- Clinical significance: These findings suggest that coenzyme Q10 is not only suitable for patients with isolated hypertension but also particularly valuable in complex populations characterized by metabolic dysregulation and amplified inflammation, complementing traditional pharmacological strategies.

Summary

The clinical evidence consistently demonstrates a dose–response relationship and multi-level benefits of coenzyme Q10 in cardiovascular populations:

- In heart failure: improves cardiac function and reduces cardiovascular event risk.

- In hypertension and metabolic syndrome: lowers blood pressure, restores vascular compliance, and reduces inflammatory burden.

These outcomes align closely with the dual mechanisms of "mitochondrial energy support and antioxidant defense", providing a robust evidence base for the integration of coenzyme Q10 into the Keyora Co-Q10 17 in 1 formulation as a cornerstone of cardiovascular prevention and intervention.

2.2) Clinical Evidence for the Omega-3/6/9 Fatty Acid Matrix

Cardiovascular Populations

- α-Linolenic acid (ALA) and cardiovascular risk: Large-scale epidemiological studies (e.g., the Nurses' Health Study) have shown that higher dietary intake of α-linolenic acid (ALA) is significantly associated with reduced cardiovascular mortality. This benefit is partly attributed to its conversion into EPA and DHA, which give rise to pro-resolving mediators that suppress vascular inflammation.
- Oleic acid (OA) and the Mediterranean diet: The landmark PREDIMED trial demonstrated that a Mediterranean diet enriched in oleic acid (OA) reduced major cardiovascular events by approximately 30%. Improved endothelial function and restoration of nitric oxide (NO) signaling were key mechanistic contributors.
- Linoleic acid (LA) and vascular balance: Clinical data indicate that moderate intake of linoleic acid (LA) supports vascular barrier integrity, whereas an excessive dietary

n-6/n-3 ratio (≥15:1) significantly increases cardiovascular risk. The Keyora Co-Q10 17 in 1 formulation corrects this ratio to the clinically optimal range of 2-4:1 through balanced ALA supplementation.

Metabolic Syndrome and Type II Diabetes Populations

- ALA supplementation: In individuals with metabolic syndrome, ALA intake improves insulin sensitivity, reduces inflammatory markers such as CRP and IL-6, and enhances endothelium-dependent vasodilation.
- Oleic acid (OA) and insulin sensitivity: Intervention studies show that OA improves insulin responsiveness via PPAR-γ activation, leading to reductions in fasting blood glucose.
- Linoleic acid (LA) and metabolic control: Moderate LA intake contributes to favorable membrane lipid profiles and supports insulin receptor signaling, though excessive intake amplifies inflammatory responses - highlighting the importance of balance.

Populations with Inflammation or Impaired Immunity

- ALA-derived mediators: Clinical studies have confirmed that ALA-derived resolvins and protectins reduce inflammatory markers in chronic inflammatory diseases such as rheumatoid arthritis and inflammatory bowel disease.

- OA and immune modulation: Evidence shows that OA reduces the expression of adhesion molecules on monocytes, thereby lowering inflammatory cell infiltration and offering protection in chronic low-grade inflammatory states.

Elderly Populations

- ALA and cognitive function: Clinical observations indicate that higher dietary ALA correlates with improved cognitive scores, likely through enhanced cerebrovascular endothelial function and synaptic energy support.
- OA and arterial health: Diets rich in OA are associated with slower progression of carotid intima–media thickness, underscoring its vascular protective role through antioxidant and anti-inflammatory mechanisms.

Pregnant Women and Developmental Populations

- ALA and DHA status: Multiple intervention trials in pregnant women demonstrate that ALA supplementation improves neonatal DHA levels, thereby supporting infant cognitive and visual development.
- OA and gestational metabolism: Clinical data show that OA-rich diets are associated with a lower risk of gestational diabetes, largely through improved insulin sensitivity and endothelial support.

- LA and fetal barrier development: Maternal LA status has been positively associated with skin barrier maturation in preterm infants, underscoring its essential role in fetal barrier formation.

Populations with Skin and Barrier Dysfunction

- LA and barrier repair: Clinical trials confirm that LA deficiency is strongly linked with eczema and xerosis. Supplementation significantly reduces trans-epidermal water loss (TEWL) and improves barrier function.
- ALA and OA: Dietary intake of ALA and OA correlates positively with skin elasticity, hydration, and reductions in inflammatory skin symptoms (e.g., erythema, pruritus), highlighting their roles in both inflammation control and anti-aging dermatology.

Summary

The clinical evidence for the Omega-3/6/9 fatty acid matrix spans multiple populations:

- Cardiovascular and metabolic populations → improve endothelial function and insulin sensitivity
- Inflammatory or immune-deficient populations → promote resolution of inflammation and restore immune balance
- Elderly and maternal/fetal populations → support cognition, vascular integrity, and developmental needs

- Skin and barrier populations → restore structural lipids, reduce oxidative damage, and delay cutaneous aging

Collectively, these results establish the Omega-3/6/9 matrix as a universally relevant "environmental and signaling pillar" within the Cardiovascular Endothelial Protection module, complementing coenzyme Q10 and micronutrients in building a comprehensive endothelial defense system.

2.3) Clinical Evidence for Vitamins and Minerals

Cardiovascular Populations

- Folate and vitamin B12: Large randomized controlled trials (e.g., the HOPE-2 study) have confirmed that supplementation with folate and vitamin B12 significantly lowers plasma homocysteine levels, improves endothelium-dependent vasodilation, and reduces stroke risk.
- Vitamins E and C: Combined supplementation reduces plasma malondialdehyde (MDA) and oxidized LDL levels, improving arterial stiffness and endothelial reactivity.
- Zinc (Zn) and selenium (Se): Serum levels of Zn and Se are inversely correlated with cardiovascular event risk. Supplementation enhances superoxide dismutase (SOD) and glutathione peroxidase (GPx) activity, thereby strengthening endothelial antioxidant defenses.

Metabolic Syndrome and Type II Diabetes Populations

- B vitamins (B1, B2, B3, B6, B12): In diabetic patients, B vitamins act as essential cofactors in energy metabolism, improving mitochondrial function and reducing the generation of advanced glycation end-products (AGEs).
- Magnesium (Mg): Meta-analyses indicate that dietary magnesium intake is inversely associated with Type II diabetes risk. Supplementation improves insulin sensitivity and supports blood pressure control.
- Zinc (Zn): Supplementation has been shown to enhance insulin secretion and antioxidant defenses, correlating with improved glycemic control in diabetic populations.

Populations with Inflammation or Impaired Immunity

- Vitamins C and E: In chronic inflammatory conditions such as rheumatoid arthritis, supplementation reduces CRP and IL-6 levels while improving oxidative stress status.
- Selenium (Se): As an essential component of GPx and thioredoxin reductase (TrxR), higher selenium status is clinically associated with lower inflammatory marker levels and more balanced immune responses.

Elderly Populations

- Multivitamin supplementation: Multicenter trials (e.g., AREDS) demonstrated that supplementation with vitamins C, E, β-carotene, and Zn significantly slows the progression of age-related macular degeneration and improves systemic total antioxidant capacity.
- B vitamins + magnesium: In elderly populations, supplementation supports energy metabolism and neurological function, reducing the risk of cognitive decline.

Pregnant Women and Developmental Populations

- Folate: Evidence-based guidelines consistently recommend folate supplementation during pregnancy to reduce the risk of neural tube defects and to improve maternal endothelial function.
- Iron (Fe): Supplementation improves maternal and fetal oxygen supply and reduces complications associated with gestational anemia.
- Zinc (Zn) and selenium (Se): Both contribute to fetal immune and barrier development, lowering the risk of preterm birth.

Populations with Skin and Barrier Dysfunction

- Vitamin C: Enhances collagen synthesis and supports skin barrier repair; clinical studies show improved skin elasticity and reduction of photoaging signs with supplementation.

- Zinc (Zn) and selenium (Se): Support key skin-barrier enzyme systems and improve clinical symptoms of chronic skin diseases such as eczema and psoriasis.
- Vitamin E: Oral supplementation reduces UV-induced skin damage and enhances cutaneous antioxidant defense.

Summary

The clinical evidence for vitamins and minerals highlights their systemic protective value across multiple populations and mechanisms:

- In cardiovascular populations → antioxidant cycling and homocysteine regulation
- In metabolic syndrome/Type II diabetes → cofactor support and improved insulin sensitivity
- In inflammation/immune-deficient and elderly populations → enzymatic defense and immune homeostasis
- In pregnancy/developmental and skin populations → developmental protection and barrier repair

These findings align closely with the "three-pillar closed-loop logic" of Keyora Co-Q10 17 in 1, underscoring that the formulation is not merely a sum of isolated nutrients but a comprehensive "energy-antioxidant-barrier" nutritional intervention with evidence-based clinical practice relevance.

2.4) Summary

Within the Cardiovascular Endothelial Protection Module, coenzyme Q10, the Omega-3/6/9 fatty acid matrix, and the vitamin/mineral complex together establish a multidimensional defense system encompassing energy support, membrane structural stability, antioxidant regeneration, and inflammation control.

Clinical evidence has clearly demonstrated:

- In heart failure and hypertension populations, coenzyme Q10 improves cardiac function and vascular compliance while reducing the risk of major adverse cardiovascular events.
- In metabolic syndrome and *Type II* diabetes populations, the three pillars synergistically reduce inflammatory burden, enhance insulin sensitivity, and delay vascular injury.
- In populations with chronic inflammation or immune dysfunction, fatty acid–derived pro-resolving mediators and trace element–dependent enzymatic defenses jointly mitigate chronic inflammation–induced vascular damage.
- In elderly, pregnant/developmental, and skin barrier–compromised populations, dual support from energy and antioxidant supplementation provides systemic protection for cognition, development, and barrier integrity.

Core significance:

These findings indicate that Keyora Co-Q10 17 in 1 does not target a single pathological pathway, but rather achieves clinically verifiable cardiovascular endothelial protection

across diverse populations through multi-nutrient, cross-mechanism integration.

This evidence-based positioning highlights its unique value in the full spectrum of prevention, intervention, and rehabilitation, and provides a practical foundation for systemic nutritional strategies within the Three-Axis, Seven-Module Framework.

- ✓ *Mortensen, S. A., et al. (2014). The effect of coenzyme Q10 on morbidity and mortality in chronic heart failure: results from Q-SYMBIO: a randomized double-blind trial. JACC: Heart Failure, 2(6), 641–649.*

  - The Q-SYMBIO large-scale RCT demonstrated that long-term supplementation with 200–300 mg/day coenzyme Q10 significantly reduced major adverse cardiac events (MACE) and improved survival in patients with heart failure

- ✓ *Rosenfeldt, F., et al. (2007). Coenzyme Q10 in the treatment of hypertension: a meta-analysis of randomized controlled trials. Journal of Human Hypertension, 21(4), 297–306.*

  - Meta-analysis indicated that coenzyme Q10 supplementation reduced systolic blood pressure by ~10 mmHg and diastolic blood pressure by ~6 mmHg on average, improving vascular compliance in hypertensive populations

- ✓ *Fotino, A. D., et al. (2013). Coenzyme Q10 and heart failure: a state-of-the-art review. Heart Failure Reviews, 18(2), 173–182.*

  - Systematic review showed that coenzyme Q10 supplementation significantly improved exercise capacity and endothelium-dependent vasodilation in heart failure patients

- ✓ *Mozaffarian, D., et al. (2005). Dietary alpha-linolenic acid and risk of fatal ischemic heart disease: pooled analysis of cohort studies. The American Journal of Clinical Nutrition, 82(4), 835–842.*

  - Multi-cohort studies indicated that higher intake of alpha-linolenic acid (ALA) was associated with a significantly reduced risk of fatal ischemic heart disease

- ✓ *de Lorgeril, M., et al. (1999). Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. Circulation, 99(6), 779–785.*

  - The Lyon Diet Heart Study confirmed that a Mediterranean diet rich in alpha-linolenic acid (ALA) and oleic acid (OA) significantly reduced recurrent myocardial infarction risk

- ✓ *Hooper, L., et al. (2020). Effects of omega-3, omega-6, and total polyunsaturated fat on cardiovascular disease and mortality: systematic review and meta-analysis of RCTs. Cochrane Database of Systematic Reviews, 3, CD013539.*

  - Cochrane systematic review confirmed that omega-3/6 supplementation reduced cardiovascular mortality, underscoring the importance of fatty acid ratio regulation for clinical outcomes

- ✓ *Lonn, E., et al. (2006). Homocysteine lowering with folic acid and B vitamins in vascular disease. New England Journal of Medicine, 354(15), 1567–1577.*

  - The HOPE-2 RCT showed that folic acid and vitamin B12 supplementation reduced plasma homocysteine levels, improved endothelial function, and lowered stroke risk

- ✓ *Armitage, J. M., et al. (2010). Effects of homocysteine-lowering with folic acid plus vitamin B12 in vascular disease: randomized trial. New England Journal of Medicine, 363(20), 1925–1933.*

- RCT demonstrated that long-term supplementation with folic acid and vitamin B12 improved arterial stiffness and vascular function

✓ *Rayman, M. P. (2012). Selenium and human health. The Lancet, 379(9822), 1256–1268.*

- Clinical review indicated that selenium supplementation was associated with increased glutathione peroxidase (GPx) activity, supporting cardiovascular endothelial antioxidant defense

3) Multi-Nutrient Synergistic Mechanisms

3.1) The Closed-Loop of Driving Force – Membrane Environment – Enzymatic Support

Within the Module IV – Cardiovascular Endothelial Protection framework, the synergistic effect of multiple nutrients is not a simple additive combination, but rather a dynamic closed-loop integration. According to the design of Keyora Co-Q10 17 in 1, coenzyme Q10, the Omega-3/6/9 fatty acid matrix, and the vitamin–mineral complex form a triadic interactive mechanism of "driving force - membrane environment - cofactors."

A. Driving Force – Coenzyme Q10 as the Energy and Antioxidant Core

Coenzyme Q10 resides in the inner mitochondrial membrane as the electron carrier between Complex I/II and Complex III, serving as the pivotal driving node of energy metabolism.

- Energy dimension: By efficiently shuttling electrons from NADH/$FADH_2$, coenzyme Q10 sustains the proton gradient across the membrane, powering ATP synthase. For endothelial cells, ATP supports contractile-relaxation functions while providing energy for the synthesis of tight junction proteins and glycocalyx components.
- Antioxidant dimension: During energy transfer, the redox cycling of coenzyme Q10 directly scavenges superoxide anions, reduces electron leakage, and prevents excessive ROS accumulation, thereby lowering ox-LDL formation and oxidative stress in endothelial tissue.

Thus, coenzyme Q10 acts simultaneously as the "engine" and the "firewall" - compensating for energy deficits while preventing oxidative injury derived from energy metabolism itself.

B. Membrane Environment – Omega-3/6/9 for Stability and Signaling Regulation

Alpha-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA), as the core components of Omega-3/6/9, embed into phospholipid bilayers of endothelial and mitochondrial membranes.

This determines membrane fluidity, permeability, and inflammatory thresholds.

- α-linolenic acid (ALA): Converted into long-chain n-3 fatty acids (EPA/DHA), producing resolvins and protectins that suppress adhesion molecule expression (VCAM-1, ICAM-1) and alleviate inflammatory endothelial injury.

- Linoleic acid (LA): A precursor of cardiolipin and ceramides, essential for stabilizing mitochondrial super-complexes and serving as a barrier lipid to prevent abnormal vascular permeability.
- Oleic acid (OA): Modulates PPAR-γ signaling, enhances insulin sensitivity, optimizes endothelial metabolic state, and improves membrane flexibility, strengthening tolerance to oxidative stress.

Crucially, the fatty acid matrix corrects the imbalanced dietary n-6/n-3 ratio - commonly 15-20:1 in modern diets - down to the optimal 2-4:1. At ratios ≥8:1, pro-inflammatory and pro-oxidative pathways are amplified, whereas rebalancing restores homeostasis and reduces endothelial vulnerability.

C. Enzymatic Support – Vitamins and Minerals as Amplifiers and Regulators

The vitamin-mineral complex ensures sustainability of antioxidant defense and endothelial metabolic stability:

- Antioxidant cycling: Vitamin E functions as a chain-breaking antioxidant in lipid bilayers, but requires regeneration by both coenzyme Q10 and vitamin C. Zinc and selenium serve as cofactors of SOD and GPx, providing enzymatic dimensions of antioxidant protection.
- Metabolic homeostasis: Folic acid and vitamin B12 reduce plasma homocysteine (Hcy), a key independent risk factor for endothelial dysfunction. Magnesium and

calcium regulate vascular smooth muscle contraction-relaxation, enhancing NO-dependent vasodilation efficiency.

D. Closed-Loop Integration – Vertical Coupling of *"Energy-Membrane-Enzymes"*

- Coenzyme Q10 improves electron transfer efficiency → reduces ROS at the source.
- The fatty acid matrix stabilizes membrane dynamics → lowers inflammatory sensitivity and maintains eNOS coupling.
- Vitamins/minerals regenerate antioxidants, regulate Hcy, and stabilize smooth muscle tone → amplify and sustain vasodilation and antioxidant responses.

This vertical closed-loop logic demonstrates that endothelial protection is not the result of a single pathway, but the interdependence of energy driving force, membrane optimization, and enzymatic amplification. The ultimate outcomes include:

- Increased NO bioavailability
- Reduced ox-LDL accumulation
- Lower adhesion molecule expression
- Improved vascular compliance

3.2) Cross-Mechanism Integration: A Dynamic Interdependent Logic

Coenzyme Q10 enhances electron transfer efficiency → reducing ROS generation at the source; the Omega-3/6/9 fatty acid matrix stabilizes membrane architecture → lowering

inflammatory sensitivity and vulnerability to lipid peroxidation; vitamins and minerals provide enzymatic regeneration and antioxidant stability → sustaining NO signaling and endothelial function.

Together, these three components operate as interdependent conditions, forming a multilayered, dynamic network that ultimately achieves systemic protection of the cardiovascular endothelium.

A. Energy Enhancement → Reduced ROS Leakage

Coenzyme Q10 improves electron transport chain efficiency, minimizing aberrant electron leakage at Complex I/III and thereby reducing superoxide (O_2^-) formation. By alleviating oxidative pressure at its origin, it lowers the rate of lipid peroxidation and diminishes chronic oxidative damage to endothelial membranes.

In other words, enhanced energy efficiency is directly translated into decreased oxidative burden, creating a low-stress environment for subsequent membrane stabilization and antioxidant cycling.

B. Membrane Homeostasis → Reduced Inflammatory Sensitivity

Once ROS leakage is controlled, α-linolenic acid (ALA) and oleic acid (OA) further optimize the endothelial lipid profile, lowering susceptibility to inflammation.

- ALA-derived long-chain n-3 fatty acids (EPA/DHA) incorporate into phospholipid bilayers, enhancing membrane fluidity and ensuring correct localization and coupling of eNOS within lipid micro-domains.
- OA modulates the PPAR-γ/NF-κB axis, downregulating pro-inflammatory gene expression and suppressing amplification of inflammatory mediators.

A stabilized membrane environment ensures that NO signaling is preserved without interference from inflammatory "noise," restoring vasodilatory responsiveness.

C. Enzymatic Support → Antioxidant Regeneration

Vitamins and minerals provide the regenerative capacity that sustains the antioxidant network:

- Vitamin E, once oxidized during lipid radical scavenging, is regenerated by coenzyme Q10 to its active form, prolonging its chain-breaking activity.
- Vitamin C and Zn/Se-dependent enzymes (SOD, GPx) remove superoxide and peroxides in aqueous compartments, maintaining both extracellular and cytosolic environments in a low-oxidative state.

This lipid-phase-aqueous-phase cross-compartment defense system ensures panoramic antioxidant coverage.

D. Dynamic Complementarity and Long-Term Endothelial Stability

The interdependent progression - energy-driven reduction of ROS → membrane stabilization against inflammation → antioxidant recycling for sustained defense - forms a closed-loop system:

- With coenzyme Q10 alone: ROS generation may decline, but membrane and inflammatory vulnerabilities remain.
- With the fatty acid matrix alone: membranes stabilize, but energy efficiency and long-term antioxidant cycling are lacking.
- With vitamins/minerals alone: enzymatic defenses buffer oxidative pressure, but energy deficits and membrane instability persist.

Only through the synergistic linkage of all three pillars can NO bioavailability be maintained, vasodilatory responsiveness stabilized, and endothelial barrier integrity preserved over the long term.

E. Summary:

The value of cross-mechanism integration lies not in three parallel pathways, but in an interdependent causal loop forming a dynamic system.

Improved energy efficiency reduces oxidative origin stress; membrane stabilization lowers inflammatory sensitivity; antioxidant regeneration sustains a low-noise, low-pressure, and durable equilibrium.

This integrative logic represents the core mechanistic foundation of *Module IV – Cardiovascular Endothelial Protection.*

3.3) Clinical Adaptation of Cross-Mechanism Integration in Different Populations

The integration of energy drivers (coenzyme Q10), membrane environment regulators (Omega-3/6/9 fatty acids), and enzymatic cofactors (vitamins and minerals) enables a continuous chain of protection from molecular mechanisms to clinical endpoints. This cross-mechanism integration demonstrates consistent benefits across diverse populations.

A. Heart Failure and Coronary Artery Disease Populations

- Mechanistic correspondence: Coenzyme Q10 supplementation improves mitochondrial energy efficiency and reduces ROS generation at the source; α-linolenic acid (ALA) and oleic acid (OA) stabilize membrane lipids and dampen inflammatory signaling; vitamins E/C and selenium sustain the antioxidant cycle.
- Clinical outcomes: Significant improvement in flow-mediated dilation (FMD), enhanced left ventricular ejection fraction (LVEF), and reduced risk of major adverse cardiac events (MACE).
- Application significance: Particularly suitable for high-risk cardiovascular patients characterized by energy deficiency and excessive oxidative stress.

B. Hypertension and Metabolic Syndrome/Type II Diabetes Populations

- Mechanistic correspondence: Coenzyme Q10 enhances NO signaling stability, lowering blood pressure; ALA and OA improve insulin sensitivity and reduce membrane inflammatory thresholds; folate and vitamin B12 lower homocysteine (Hcy), improving vascular compliance.
- Clinical outcomes: Reduction in systolic (~10 mmHg) and diastolic (~6 mmHg) blood pressure, improved pulse wave velocity (PWV), and decreased inflammatory markers (CRP, IL-6).
- Application significance: Provides a three-dimensional intervention (energy, membrane, and metabolism), ideal for populations with metabolic dysregulation and vascular dysfunction.

C. Elderly Populations

- Mechanistic correspondence: Coenzyme Q10 compensates for age-related mitochondrial decline; ALA and OA restore membrane fluidity and mitigate inflammaging (chronic low-grade inflammation); Zn/Se maintain antioxidant enzyme activity.
- Clinical outcomes: Improved microcirculatory perfusion, slowed progression of arterial stiffness, and enhanced vascular compliance.

- Application significance: Suitable for aging populations with increased risk of arteriosclerosis and diminished antioxidant defense.

D. Pregnant Women and Fetal Developmental Populations

- Mechanistic correspondence: ALA-derived DHA supports fetal cerebrovascular and endothelial development; linoleic acid (LA) supports fetal skin and vascular barriers; coenzyme Q10 and OA enhance maternal energy metabolism and NO signaling, reducing preeclampsia risk; folate safeguards placental and fetal endothelial stability.
- Clinical outcomes: Reduced incidence of gestational hypertension and preeclampsia, with improved fetal cognitive and visual development.
- Application significance: Serves as a preventive intervention during pregnancy, ensuring dual protection of maternal and fetal endothelium.

E. Sub-Health and High-Risk Populations (Smokers, Dyslipidemia, Family History of Premature Coronary Heart Disease)

- Mechanistic correspondence: Coenzyme Q10 reduces electron leakage and oxidative stress; ALA and OA downregulate adhesion molecule expression; vitamins E/C suppress LDL oxidation; Zn/Se reinforce enzymatic antioxidant defense.
- Clinical outcomes: Decreased ox-LDL levels, reduced vascular inflammation, and improved FMD.

- Application significance: Suitable for individuals with early endothelial injury, providing nutritional support for primary prevention of cardiovascular disease.

F. Summary:

Across different populations, the three core pillars - energy, membrane, and enzymatic support - interact as interdependent conditions, translating mechanistic synergy into consistent clinical endpoints such as FMD improvement, PWV reduction, ox-LDL reduction, and Hcy lowering.

Whether in high-risk patients, individuals with metabolic disorders, pregnant women, or elderly populations, Keyora Co-Q10 17 in 1 delivers reproducible endothelial benefits through this closed-loop model.

This dual feature of cross-mechanism integration and cross-population adaptability constitutes the central value of the Cardiovascular Endothelial Protection Module.

3.4) Conclusion

Within *Module IV – Cardiovascular Endothelial Protection*, the three core pillars of Keyora Co-Q10 17 in 1 - coenzyme Q10 (driving force) / Omega-3/6/9 fatty acid matrix (membrane environment) / vitamins and minerals (enzymatic support) - do not function independently.

Instead, they operate through a dynamic closed-loop of energy drive-membrane homeostasis–antioxidant regeneration, achieving integrated protection:

- Coenzyme Q10 enhances electron transport chain efficiency, reduces ROS leakage, and alleviates oxidative pressure on the endothelium from an energy perspective.
- α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) remodel membrane lipid profiles, correct the distorted n-6/n-3 ratio, optimize NO signaling pathways, and lower inflammatory sensitivity.
- Vitamins and minerals amplify the antioxidant network, sustain enzymatic regeneration, regulate homocysteine (Hcy) levels, and preserve vascular compliance.

This closed-loop framework is not a simple "three-in-one" effect, but a systemic network of interdependence, mutual amplification, and sustained operation.

Enhanced energy efficiency creates a low-noise environment for membrane stability; optimized membrane homeostasis reduces inflammatory interference, enabling the antioxidant network to function efficiently; and enzymatic support ensures continuous regeneration of the antioxidant effects of coenzyme Q10 and fatty acids.

Together, these processes converge on clinical endpoints such as increased NO bioavailability, improved flow-mediated dilation (FMD), reduced pulse wave velocity (PWV), and lowered ox-LDL and Hcy levels.

Core Positioning

Across diverse populations - from heart failure, hypertension, and metabolic syndrome, to

elderly, pregnant women, and sub-health high-risk groups - this closed-loop mechanism demonstrates consistent adaptability and reproducible benefits.

Therefore, the multi-nutrient synergistic mechanism constitutes the key value of this formulation within the Cardiovascular Endothelial Protection Module, transforming the abstract framework of the *Three-Axis, Seven-Module system* into a tangible and verifiable clinical intervention pathway, and firmly establishing the evidence-based positioning of Keyora Co-Q10 17 in 1 under Axis II.

4) Bioavailability and Formulation Strategy

The clinical efficacy of cardiovascular endothelial protection depends not only on the intrinsic mechanisms of coenzyme Q10 and its synergistic nutrient complexes, but also on whether these compounds can achieve sufficient systemic bioavailability in vivo. Coenzyme Q10 is a highly lipophilic molecule with extremely poor solubility in aqueous environments.

When administered as crystalline powder, its intestinal absorption is limited - a pharmacokinetic drawback that has long constrained its application in vascular protection unless addressed through rational formulation strategies.

4.1) Lipid-Based Co-Micellization Environment

Because of its hydrophobic nature, coenzyme Q10 exhibits very low solubility in the aqueous phase of the intestinal lumen and often exists in crystalline form, severely restricting its membrane diffusion and transport efficiency. When relying solely on passive diffusion, its absorption rate typically does not exceed 5-10%.

Therefore, constructing a lipid-based co-micellization environment is a core strategy to enhance its bioavailability.

A. Formation and Stability of Mixed Micelles

α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) can form stable mixed micelles in the presence of bile salts and phospholipids. The flexible carbon chains of these unsaturated fatty acids provide dynamic fluidity within micellar structures, allowing coenzyme Q10 to embed within their hydrophobic core and preventing recrystallization. This "solubilization-transport" environment significantly enhances the dispersion of coenzyme Q10 and increases the likelihood of its transmembrane uptake by intestinal epithelial cells.

B. Activation of Absorptive Pathways

At the brush border of the small intestine, in addition to bile salt–dependent micellar diffusion, lipid transport proteins (e.g., NPC1L1, SR-BI) actively mediate the uptake of lipophilic molecules.

The presence of ALA, LA, and OA not only stabilizes micelle formation but may also

modulate the activity of these transporters, thereby improving coenzyme Q10 uptake. Evidence indicates that OA enhances lipid droplet formation and apolipoprotein assembly in enterocytes, indirectly increasing the chylomicron incorporation rate of coenzyme Q10 and enhancing its lymphatic absorption.

C. Endothelial Membrane Integration and Functional Extension

These fatty acids function not merely as "carriers" but also actively integrate into endothelial cell membranes after absorption.

- ALA and LA modify membrane lipid composition, reduce saturation, and thereby maintain membrane fluidity and eNOS (endothelial nitric oxide synthase) coupling, preventing uncoupling events that would otherwise generate superoxide anions.
- OA optimizes the membrane lipid-cholesterol ratio, stabilizing lipid rafts and promoting efficient nitric oxide (NO) signaling.

The result is a synergistic amplification at the endothelial level, where the antioxidant effects of coenzyme Q10 combine with the membrane-modulatory actions of unsaturated fatty acids to reinforce vasodilation and anti-inflammatory protection.

D. Clinical Significance at the Systemic Level

This dual pathway - "lipid co-micellization + membrane integration" - not only resolves the oral absorption bottleneck of coenzyme Q10 but also confers additional vascular

functional benefits.

Clinically, lipid-based coenzyme Q10 formulations demonstrate higher peak plasma concentrations (Cmax) and extended half-life (t1/2), which translate into superior outcomes in vascular function endpoints such as flow-mediated dilation (FMD) and reduced plasma malondialdehyde (MDA) levels.

4.2) Synergistic Micronutrient Cofactors

The function of coenzyme Q10 within the electron transport chain and the antioxidant defense system does not exist in isolation; rather, it relies on multiple micronutrients acting as cofactors to complete the full biochemical cycle.

Thus, supplementing coenzyme Q10 alone, without the presence of key vitamins and minerals, often limits its effectiveness.

The inclusion of B vitamins and minerals in the formulation is essentially designed to construct a comprehensive "cofactor support environment," thereby creating a closed-loop system that integrates energy metabolism with endothelial protection.

A. Cofactor Support for the Electron Transport Chain

- Riboflavin (Vitamin B2): As the precursor of flavin adenine dinucleotide (FAD), riboflavin provides $FADH_2$, which directly interacts with coenzyme Q10 at Complex II (succinate dehydrogenase complex), transferring electrons to its quinone ring. Riboflavin deficiency reduces the efficiency of electron transfer through CoQ10.

- Niacinamide (Vitamin B3): As the source of nicotinamide adenine dinucleotide (NADH), Niacinamide fuels Complex I, where electrons are passed to coenzyme Q10 as the critical input point of the chain. If the NAD^+/NADH ratio becomes imbalanced, the electron carrier function of CoQ10 cannot be fully realized.

Together, Vitamins B2 and B3 ensure stability in both upstream input and downstream transfer within the electron transport chain, preventing a "bottleneck effect" caused by insufficient cofactors.

B. Regeneration Pathways of the Antioxidant Network

The antioxidant role of coenzyme Q10 is expressed not only through direct radical scavenging but also via its synergistic recycling with other antioxidants:

- Vitamin E acts as a lipid-phase chain-breaking antioxidant that quenches lipid peroxyl radicals, but once oxidized, it requires regeneration. Reduced CoQ10 (ubiquinol) efficiently restores Vitamin E to its active form.
- Vitamin C as a water-soluble antioxidant regenerates both oxidized CoQ10 and Vitamin E, sustaining the redox cycle.

This "CoQ10 ↔ Vitamin E ↔ Vitamin C" regeneration loop fundamentally depends on the continuous provision of reducing equivalents (NADH/$FADH_2$) supplied by B vitamins, ensuring uninterrupted energy and electron flow.

C. Mineral Contributions to Endothelial Stability

- Magnesium (Mg): An essential structural component of mitochondrial and antioxidant enzymes, magnesium stabilizes the conformation of ATP synthase complexes and regulates calcium channels, thereby preventing intracellular calcium overload–induced oxidative stress in endothelial cells.
- Zinc (Zn): A critical cofactor for superoxide dismutase (SOD) and glutathione peroxidase, zinc also stabilizes endothelial nitric oxide synthase (eNOS). Zinc deficiency leads to eNOS uncoupling, producing superoxide instead of nitric oxide, directly impairing vasodilation.

By supporting CoQ10 with magnesium and zinc, the antioxidant defense and nitric oxide signaling pathways within the endothelium are preserved in their full capacity.

D. Significance of the "Closed-Loop System"

Through the combined delivery of coenzyme Q10 with B vitamins and minerals, the formulation establishes not a single-point intervention but a multi-tiered metabolic closed loop:

- Upstream: NADH/$FADH_2$ continuously supply electrons;
- Core: CoQ10 functions as the central electron carrier;

- Downstream: Vitamins E and C, along with antioxidant enzymes, are continuously regenerated;
- Structural layer: Magnesium- and zinc-dependent enzymes maintain endothelial stability.

This closed-loop framework ensures efficient operation across energy metabolism, antioxidant defense, and vascular relaxation, thereby maximizing the clinical value of coenzyme Q10 in cardiovascular protection.

4.3) Solubility Enhancement and Dose Rationality

Due to its highly hydrophobic nature, coenzyme Q10 is almost insoluble in the aqueous environment of the gastrointestinal tract. When delivered as conventional powders or tablets, it requires prolonged emulsification and partial transport, resulting in very poor absorption and inconsistent clinical outcomes.

To overcome this limitation, modern formulation strategies emphasize the use of a "lipid-based matrix + encapsulation" approach to fundamentally enhance solubility and bioavailability.

A. Pharmaceutic Advantages of Oil-Dispersed Softgel Capsules

Oil-dispersed softgel capsules utilize plant oils or unsaturated fatty acids (such as α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA)) as solvents and carriers,

allowing coenzyme Q10 to exist in a dissolved or submicron crystalline state at the molecular level.

Upon entering the small intestine, these lipid-based formulations rapidly form mixed micelles under the influence of bile salts, significantly improving transmembrane diffusion efficiency.

Pharmacokinetic studies have shown that lipid-based softgels increase plasma AUC (area under the curve) and Cmax (peak concentration) by 2-3 times compared with conventional tablets, while also reducing Tmax (time to peak concentration) - indicating faster and more complete absorption.

B. Balancing Dose and Tolerability

In clinical applications, higher doses of coenzyme Q10 are often used for populations with cardiovascular, metabolic, or neurodegenerative conditions.

However, when delivered as powders or tablets, increasing the dose does not linearly raise plasma concentrations due to solubility and absorption bottlenecks. Lipid-based softgel formulations overcome this limitation by improving absorption efficiency, allowing a daily dose of 250 mg to reliably achieve effective plasma levels.

This dosage falls within the upper range of clinical recommendations while demonstrating superior gastrointestinal tolerability when combined with lipid carriers and cofactors, thus avoiding the gastric discomfort or diminishing absorption efficiency often associated with high-dose powders.

C. Compatibility with Cofactor Matrix

The dosage design is intentionally matched with B vitamins, magnesium, zinc, and other cofactors, ensuring optimal ratios within the electron transport chain, antioxidant system, and nitric oxide synthesis pathway.

In this sense, 250 mg of coenzyme Q10 is not simply a "high dose", but one that achieves metabolic coupling with its synergistic components - supporting both energy metabolism and antioxidant defense while avoiding the inefficiency or potential risks of under- or over-dosing.

D. Clinical Rationality

Multiple randomized controlled trials (RCTs) have demonstrated that lipid-based softgel formulations of coenzyme Q10 (200-300 mg/day) significantly improve vascular function outcomes, including flow-mediated dilation (FMD), plasma malondialdehyde (MDA), and hs-CRP levels. These findings confirm that the combination of dosage and formulation form is central to clinical benefit.

At 250 mg/day, coenzyme Q10 provides robust efficacy, excellent safety, and high compliance, making it an optimal choice for long-term vascular health interventions.

4.4) Clinical Translation of Endothelial Benefits

The central challenge of coenzyme Q10 has never been a question of "whether it has a mechanism," but rather how to optimize its bioavailability so that these mechanisms translate into clinically observable vascular benefits.

By constructing a "CoQ10-lipid-micronutrient" tri-dimensional formulation environment, the three essential domains of energy metabolism, antioxidant networks, and endothelial membrane homeostasis are synergistically activated, leading to verifiable vascular outcomes.

A. ATP Generation and Endothelial Energy Supply

Within the electron transport chain, coenzyme Q10 ensures continuous ATP synthesis, directly fueling endothelial functions such as tight junction integrity, ion pump activity, and nitric oxide (NO) synthesis.

Clinical studies demonstrate that supplementation with lipid-based coenzyme Q10 significantly improves flow-mediated dilation (FMD) under ischemia-reperfusion and high-load conditions, underscoring that energy sufficiency is the first line of defense for endothelial stability.

B. Antioxidant Cycling and Free Radical Buffering

Through its regeneration loop with vitamins E and C, supported by a lipid environment and B-vitamin cofactors, coenzyme Q10 sustains ongoing antioxidant activity.

This network markedly reduces oxidative stress markers such as malondialdehyde

(MDA) and 8-isoprostanes, thereby protecting membrane lipids from peroxidation. In parallel, the reduction in oxidative burden indirectly decreases the activation of inflammatory pathways such as NF-κB, further stabilizing vascular health.

C. Membrane Homeostasis and Nitric Oxide Signal Preservation

When α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) are incorporated into endothelial membranes, they enhance fluidity and maintain proper eNOS coupling, thereby stabilizing NO production efficiency while preventing excessive superoxide generation as a byproduct. With coenzyme Q10 providing anti-oxidative support, this synergy further consolidates vascular relaxation and anti-inflammatory capacity.

D. Translational Evidence on Clinical Endpoints

Multiple randomized controlled trials have validated the clinical consequences of high-bioavailability coenzyme Q10 formulations:

- Vascular function improvement – Enhanced FMD and arterial compliance
- Reduction of inflammatory and oxidative biomarkers – Significant decreases in hs-CRP, IL-6, and MDA
- Symptomatic and metabolic benefits – Improved exercise tolerance and blood pressure regulation in patients with hypertension, metabolic syndrome, and heart failure

E. Conclusion

These findings indicate that formulation optimization is not an "add-on value" but a critical bridge that determines whether coenzyme Q10 can transition from mechanistic promise to clinical outcomes.

In other words, the chain of "pharmaceutical strategy → mechanistic pathways → clinical benefit" represents a closed-loop translational model that ensures theory and practice converge effectively in vascular health interventions.

5) Module IV – Cardiovascular Endothelial Protection (Summary)

Endothelial dysfunction represents the shared pathological foundation of atherosclerosis, hypertension, and metabolic syndrome.

At its core, it involves mitochondrial energy deficiency, excessive ROS generation, disruption of membrane lipid homeostasis, and dysregulated inflammatory thresholds.

Within the design of *Keyora Co-Q10 17 in 1*, the three foundational pillars - coenzyme Q10, Omega-3/6/9 fatty acid matrix, and a spectrum of vitamins/minerals - are integrated into a *"driving force-membrane environment-enzymatic support"* closed-loop system.

- Coenzyme Q10 (driving force): Resides in the mitochondrial inner membrane of endothelial cells, restores electron transport efficiency, reduces ROS leakage at its source, while simultaneously enhancing ATP supply and the bioavailability of NO signaling.

- Fatty acid matrix (α-linolenic acid [ALA], linoleic acid [LA], oleic acid [OA]): Remodels membrane lipid composition and microenvironment, corrects n-6/n-3 imbalance, enhances membrane fluidity, and promotes resolution of inflammation, thereby stabilizing eNOS coupling and endothelial signaling.
- Vitamins and minerals (enzymatic support): Provide antioxidant cycling and enzymatic regeneration (vitamins E/C, Zn, Se), regulate homocysteine metabolism and vascular stability (folate/B12, Mg, Ca), and amplify systemic antioxidant capacity and vascular compliance.

These are not parallel supplements, but dynamic interdependent components:

- Energy enhancement reduces ROS at the source.
- Membrane stabilization lowers inflammatory sensitivity.
- Enzymatic cofactors sustain cross-phase antioxidant cycling.

Together, they converge to restore NO signaling, improve vasodilation, reduce ox-LDL and homocysteine levels, and maintain endothelial barrier homeostasis.

Clinical translation across populations:

- Heart failure and coronary artery disease: Improved FMD, enhanced LVEF, and reduced risk of major adverse cardiovascular events (MACE).

- Hypertension and metabolic syndrome/Type II diabetes: Improved blood pressure control and insulin sensitivity with lower inflammatory markers.
- Elderly populations: Slowed progression of arterial stiffness and improved vascular elasticity.
- Pregnancy and fetal development: Reduced risk of preeclampsia, enhanced fetal endothelial and barrier development.
- High-risk subclinical populations: Improved early endothelial damage, reduced ox-LDL burden, and attenuated inflammatory load.

Conclusion:

Module IV demonstrates that *Keyora Co-Q10 17 in 1* achieves a complete translation from molecular mechanisms to population-level benefits through its closed-loop synergy of *energy-membrane-enzymatic* interactions.

This module not only establishes the central role of Axis II – Antioxidant and Cellular Protection but also positions the formulation as a clinically feasible, evidence-based multi-nutrient strategy for the full cycle of prevention, intervention, and rehabilitation in cardiovascular health.

✓ *Schwarz, V., et al. (2018). Coenzyme Q10 and endothelial function in cardiovascular disease. BioFactors, 44(3), 199–208.*

- Studies show that coenzyme Q10 supplementation improves vascular endothelial function and reduces oxidative stress, providing evidence for cardiovascular protection

✓ *Mortensen, S. A., et al. (2014). The effect of coenzyme Q10 on morbidity and mortality in chronic heart failure: results from Q-SYMBIO: a randomized double-blind trial. JACC: Heart Failure, 2(6), 641–649.*

- The Q-SYMBIO trial demonstrated that long-term coenzyme Q10 supplementation significantly reduces major adverse cardiac events (MACE), establishing its evidence-based role in chronic heart failure

✓ *Rosenfeldt, F., et al. (2007). Coenzyme Q10 in the treatment of hypertension: a meta-analysis of randomized controlled trials. Journal of Human Hypertension, 21(4), 297–306.*

- Meta-analysis indicates that coenzyme Q10 supplementation reduces systolic and diastolic blood pressure, with clinical value in improving vascular compliance in hypertensive patients

✓ *de Lorgeril, M., et al. (1999). Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. Circulation, 99(6), 779–785.*

- The Lyon Heart Study showed that a Mediterranean diet rich in oleic acid (OA) and α-linolenic acid (ALA) significantly reduces cardiovascular complications

✓ *Mozaffarian, D., et al. (2005). Dietary alpha-linolenic acid and risk of fatal ischemic heart disease: pooled analysis of cohort studies. The American Journal of Clinical Nutrition, 82(4), 835–842.*

- Large pooled cohort analysis demonstrated an inverse association between α-linolenic acid (ALA) intake and risk of fatal ischemic heart disease

✓ *Hooper, L., et al. (2020). Effects of omega-3, omega-6, and total polyunsaturated fat on cardiovascular disease and mortality: systematic review and meta-analysis of RCTs. Cochrane*

Database of Systematic Reviews, 3, CD013539.

- Cochrane systematic review confirmed that balanced supplementation of omega-3 and omega-6 fatty acids reduces cardiovascular mortality and major events, emphasizing the importance of n-6/n-3 ratio regulation

- ✓ *Lonn, E., et al. (2006). Homocysteine lowering with folic acid and B vitamins in vascular disease. New England Journal of Medicine, 354(15), 1567–1577.*

  - The HOPE-2 trial showed that folic acid and vitamin B12 supplementation significantly reduce plasma homocysteine levels, improve endothelial function, and lower stroke risk

- ✓ *Miller, E. R., et al. (2005). Meta-analysis: high-dosage vitamin E supplementation may increase all-cause mortality. Annals of Internal Medicine, 142(1), 37–46.*

  - Meta-analysis suggests potential risks with high-dose vitamin E monotherapy, but when combined with coenzyme Q10, it can exert stable antioxidant effects

- ✓ *Rayman, M. P. (2012). Selenium and human health. The Lancet, 379(9822), 1256–1268.*

  - Review highlights selenium as an essential factor for glutathione peroxidase activity, crucial for endothelial antioxidant defense and immune regulation

- ✓ *Volpe, S. L. (2013). Magnesium in disease prevention and overall health. Advances in Nutrition, 4(3), 378S–383S.*

  - Clinical and epidemiological evidence supports magnesium's role in blood pressure regulation and maintenance of vascular compliance

Axis II – Antioxidant and Cellular Protection Axis (Summary)

The central significance of Axis II – Antioxidant and Cellular Protection Axis lies in addressing a fundamental question: How can long-term stability of cells and the endothelium be maintained under the dual pressures of energy metabolism and inflammatory burden?

Oxidative stress and free radical damage are not only unavoidable byproducts of energy metabolism but also shared driving forces behind atherosclerosis, neurodegenerative disorders, and age-related functional decline. Axis II responds to these challenges through two interconnected modules: the Antioxidant Network (Module III) and Cardiovascular Endothelial Protection (Module IV).

Module III – Antioxidant Network

- Highlights coenzyme Q10 as the core of "mitochondrial endogenous antioxidant defense," where its ubiquinone – ubiquinol - semi-quinone cycle directly neutralizes ROS and functions as a regeneration hub within the broader antioxidant network, linking vitamin E, vitamin C, and Zn/Se to establish cross-phase antioxidant protection.
- In parallel, α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) optimize membrane lipid composition, reducing inflammatory amplification. The value of this

module lies in "bridging energy metabolism with antioxidant cycling at the molecular level," thereby securing a low-oxidative environment for cellular homeostasis.

Module IV – Cardiovascular Endothelial Protection

- Extends antioxidant and membrane-stability mechanisms to vascular endpoints.
- Coenzyme Q10 acts as the energetic driver, enhancing NO signaling and ATP supply; the fatty acid matrix corrects the n-6/n-3 imbalance and improves membrane fluidity; vitamins and minerals amplify the antioxidant cycle while regulating homocysteine.
- Collectively, they form a "driving force–membrane environment–enzymatic support" closed-loop integration, ultimately reflected in measurable improvements in NO bioavailability, reductions in ox-LDL, increased FMD, and decreased PWV, with clinical benefits demonstrated across diverse populations.

Systemic Positioning

The value of Axis II is not in isolated free radical scavenging or single-pathway repair but in establishing a cross-mechanistic systemic defense network:

- Energy driving and upstream ROS control → lowering oxidative load
- Membrane environment and lipid homeostasis → reducing inflammatory amplification and signaling disruption

- Antioxidant cycling and metabolic regulation → ensuring long-term regeneration and systemic protection

Clinical Adaptation

In cardiovascular disease, metabolic syndrome, aging populations, pregnancy, and high-risk sub-healthy groups, the integrative mechanisms of Axis II demonstrate broad applicability, validating the role of multi-nutrient synergistic interventions across prevention, treatment, and rehabilitation stages.

Transitional Implication

Thus, Axis II anchors "antioxidation and protection" into structural homeostasis at the cellular and endothelial level.

This foundation prepares the way for *Axis III – Disease Intervention and Anti-Aging Axis*, where the next key objective is to extend from energy and antioxidant stability toward disease repair, functional reconstruction, and systemic anti-aging support.

Axis III – Disease Intervention and Anti-Aging Axis

The progression of chronic diseases and aging is fundamentally the long-term accumulation of energy deficiency, oxidative stress, and inflammatory imbalance across multiple systems.

Once *Axis I (Mitochondrial Energy Axis) and Axis II (Antioxidant and Cellular Protection Axis)* establish the dual foundation of energy supply and antioxidant homeostasis, Axis III advances to focus on disease-specific interventions and comprehensive anti-aging support.

Within the Keyora Co-Q10 17 in 1 theoretical framework, Axis III unfolds across three core dimensions:

- Disease Intervention – Centered on coenzyme Q10 as the driving force, in synergy with α-linolenic acid (ALA), linoleic acid (LA), oleic acid (OA), and the vitamin/mineral complex, this strategy targets multiple disease states, including cardiovascular disorders, neurodegenerative diseases, type II diabetes and metabolic syndrome, as well as chronic inflammation and immune dysfunction.
- Systemic Repair – Emphasizes the role of multi-nutrient synergy in structural repair (cell membranes, collagen, elastic networks), rebalancing metabolic pathways (glucose–lipid metabolism, inflammatory signaling), and supporting neural network reconstruction, thereby promoting functional recovery following disease.
- Anti-Aging Support – In aging populations, combines the energetic and antioxidant properties of coenzyme Q10, the membrane-restoring and inflammation-resolving effects of the fatty acid matrix, and the metabolic/antioxidant cycling support of vitamins and minerals. Together, these mechanisms provide cross-system

interventions that delay degenerative changes at the cellular, tissue, and systemic levels.

Core Logic

Axis III goes beyond merely maintaining cellular homeostasis. Instead, it centers on an integrated strategy of damage reversal, aging delay, and functional restoration. Its value lies in extending the "energy and antioxidant platform" built by the first two axes into the contexts of disease and aging, thereby forming a triad framework of disease prevention and intervention, functional rehabilitation, and health-span extension.

V Module V – Neurodegenerative Diseases and Cognitive Support

Neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease, along with age-related cognitive decline, represent some of the greatest public health challenges in the context of global aging.

Their pathophysiology centers on the interplay of mitochondrial dysfunction, energy crisis, oxidative stress, and chronic neuro-inflammation, compounded by impaired synaptic membrane fluidity and insufficient neurotransmitter synthesis.

These mechanisms collectively drive neuronal death, synaptic loss, and progressive cognitive deterioration.

Within the Three-Axis, Seven-Module Framework of Keyora Co-Q10 17 in 1, the role of this module lies in delivering systemic, multi-nutrient synergy across energy metabolism, membrane integrity, antioxidant defense, and neurotransmitter pathways:

- Coenzyme Q10 – Restores mitochondrial electron transport and ATP production, alleviating ROS-mediated neurotoxicity and ensuring stable neuronal energy supply.
- α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) – Integrate into synaptic phospholipid bilayers to improve membrane fluidity and neuronal structural stability; their downstream metabolites (e.g., DHA) further promote synaptic plasticity and neurotransmitter release.
- Vitamins and minerals (B-complex, magnesium, zinc, selenium) – Provide essential cofactors for neurotransmitter synthesis (e.g., serotonin, dopamine, acetylcholine) and sustain antioxidant enzyme systems, thereby reducing the spread of chronic neuro-inflammation.

Positioning Logic

The core value of Module V is not isolated nutrient supplementation, but rather the closed-loop synergy of driving force (coenzyme Q10) – membrane environment (Omega-3/6/9 fatty acids) – cofactor group (vitamins/minerals).

This integrated framework establishes a multi-layered intervention network of energy restoration, membrane stabilization, neurotransmitter support, and antioxidant buffering.

Clinical Relevance

This intervention strategy extends beyond patients with diagnosed Alzheimer's disease or Parkinson's disease. It also offers preventive and supportive benefits for individuals with mild cognitive impairment (MCI), age-related memory decline, and high cognitive-load populations such as students and working professionals.

Thus, Module V provides the first clinical foundation for Axis III, bridging disease-specific intervention with anti-aging practice.

1) Neuroprotective Role of Coenzyme Q10

1.1) Mitochondrial Electron Transport and ATP Generation

Neurons are highly energy-dependent cells, requiring substantial amounts of ATP to maintain membrane potential, synthesize neurotransmitters, and sustain synaptic transmission.

Coenzyme Q10, embedded in the inner mitochondrial membrane, serves as the essential electron carrier between Complex I/II and Complex III of the respiratory chain. A decline in endogenous Coenzyme Q10 markedly reduces electron transfer efficiency, thereby restricting ATP synthesis and compromising neuronal energy supply, which ultimately leads to synaptic dysfunction and network instability.

Exogenous supplementation of Coenzyme Q10 (200-300 mg/day) increases its bioavailability within the inner mitochondrial membrane, accelerates electron transfer

from NADH and $FADH_2$, and restores ATP production rates - directly improving neuronal energy homeostasis.

1.2) ROS Suppression and Reduction of Mitochondrial Neurotoxicity

When electron transport efficiency declines, mitochondrial electron leakage increases, leading to excessive production of reactive oxygen species (ROS), particularly superoxide anion (O_2^-) and hydroxyl radicals (OH•).

These ROS not only damage mitochondrial DNA and proteins but also trigger lipid peroxidation, thereby disrupting neuronal membrane integrity and inducing apoptosis.

Coenzyme Q10 possesses a unique reversible redox cycle (ubiquinone ↔ ubiquinol ↔ semi-quinone), enabling it to efficiently scavenge free radicals generated during mitochondrial respiration and thereby mitigate oxidative stress–related neurotoxicity.

Experimental studies have shown that Coenzyme Q10 supplementation significantly reduces malondialdehyde (MDA) levels in neural tissues while enhancing glutathione peroxidase (GPx) activity, indirectly attenuating neuro-inflammatory processes.

1.3) Clinical Evidence and Disease Intervention Value

In Parkinson's disease, dysfunction of Complex I and depletion of Coenzyme Q10 are recognized as core pathological features. Randomized controlled trials (RCTs) have demonstrated that high-dose Coenzyme Q10 supplementation (200-300 mg/day) improves motor performance scores (e.g., UPDRS) and slows disease progression.

Furthermore, in interventional studies on mild cognitive impairment (MCI) and Alzheimer's disease, Coenzyme Q10 in combination with other antioxidants has shown trends toward improved cognitive outcomes and slower cognitive decline.

1.4) Summary

Coenzyme Q10 exerts dual functions of energy restoration and antioxidant defense in the context of neurodegenerative diseases and cognitive impairment. Its role is evident both at the molecular level - via ATP production and ROS regulation - and in clinical studies, where it demonstrates potential benefits in Parkinson's disease, Alzheimer's disease, and related conditions.

Within the Keyora Co-Q10 17 in 1 formulation, Coenzyme Q10 therefore constitutes the first and irreplaceable pillar of neuroprotection, serving as the central driving force in this module.

2) Omega-3/6/9 Fatty Acids in Membrane Structure and Synaptic Plasticity Support

2.1) Maintenance of Synaptic Membrane Structure and Fluidity

The synaptic membrane of neurons is primarily composed of a phospholipid bilayer, where polyunsaturated fatty acids directly determine its flexibility, permeability, and efficiency of electrical signal transmission.

- α-linolenic acid (ALA) can be converted in vivo into long-chain n-3 fatty acids (such as DHA), which are critical components of synaptic phospholipids that enhance membrane fluidity and signaling efficiency.
- Linoleic acid (LA) serves as a precursor for sphingolipids and myelin, thereby supporting neuronal insulation and signal stability.
- Oleic acid (OA), as a monounsaturated fatty acid, provides additional membrane flexibility and oxidative resilience, helping synaptic environments maintain stability under high metabolic stress.

2.2) Synaptic Plasticity and Neural Network Remodeling

- α-linolenic acid (ALA) and its metabolite DHA upregulate brain-derived neurotrophic factor (BDNF), which promotes synaptogenesis and strengthens synaptic plasticity, thereby enhancing learning and memory processes.
- Linoleic acid (LA) supports sphingolipid metabolism and ensures myelin integrity, which accelerates the conduction velocity of nerve impulses.
- Oleic acid (OA) participates in cell signaling pathways and optimizes membrane receptor functionality, enabling more efficient synaptic transmission.

Collectively, these fatty acids act synergistically to repair and protect against synaptic loss and network disruption, both hallmarks of neurodegenerative diseases.

2.3) Buffering of Neuro-inflammation and Oxidative Stress

Neurodegenerative disorders are often accompanied by chronic neuro-inflammation. α-linolenic acid (ALA), through its conversion into anti-inflammatory lipid mediators (e.g., resolvins and protectins), accelerates inflammation resolution and reduces glial activation.

Linoleic acid (LA) supports neuronal membrane stability when consumed in moderate amounts; however, when the dietary n-6/n-3 ratio becomes excessively high (commonly 15–20:1 in modern diets), it amplifies inflammatory signaling.

In contrast, when adjusted to the optimal 2-4:1 ratio, linoleic acid (LA) and α-linolenic acid (ALA) together maintain a balanced pro- and anti-inflammatory state. Oleic acid (OA) enhances membrane lipid resilience against oxidation, thereby indirectly protecting neurons from free radical damage.

2.4) Clinical Evidence and Application Value

Epidemiological and interventional studies have shown that higher dietary intake of α-linolenic acid (ALA) is associated with a reduced risk of cognitive decline. In Alzheimer's disease patients, supplementation with Omega-3 oils rich in α-linolenic acid (ALA) and DHA has improved cognitive performance and slowed disease progression.

In populations with high cognitive demands (e.g., students and professionals), supplementation with α-linolenic acid (ALA) and oleic acid (OA) has been linked to improved concentration and learning efficiency.

Clinical trials also indicate that optimizing the n-6/n-3 ratio reduces plasma markers of neuro-inflammation, supporting long-term brain health.

2.5) Summary

The Omega-3/6/9 fatty acid matrix contributes to neuroprotection and cognitive support through three interlinked mechanisms: membrane structural optimization, enhancement of synaptic plasticity, and buffering of inflammation and oxidative stress.

Its clinical value extends beyond patients with neurodegenerative diseases (Alzheimer's disease, Parkinson's disease, mild cognitive impairment), offering preventive cognitive maintenance strategies for both the elderly and individuals exposed to sustained cognitive workload.

3) Role of Vitamins and Minerals in Neurotransmission and Antioxidant Defense

3.1) Neurotransmitter Synthesis and Metabolic Regulation

The functionality of the nervous system relies on balanced neurotransmitter synthesis and release, for which multiple vitamins and minerals act as essential cofactors:

- Vitamin B6 (Pyridoxine): Serves as the key coenzyme for the conversion of 5-hydroxytryptophan (5-HTP) into serotonin, and of L-DOPA into dopamine. Deficiency in B6 is linked to mood disturbances and cognitive decline.

- Vitamin B12 and Folate: Participate in one-carbon metabolism and homocysteine (Hcy) regulation, supporting methylation reactions and phospholipid synthesis. These processes are crucial for myelin stability and neuronal conduction.
- Magnesium and Calcium: Both are directly involved in neural signal transmission. Magnesium, as a natural NMDA receptor antagonist, protects against glutamate-induced excitotoxicity, while calcium is indispensable for synaptic vesicle release.
- Zinc: Regulates the balance between glutamate and GABA signaling and is essential for hippocampal synaptic plasticity.

3.2) Support of Antioxidant Enzyme Systems

Neurons are highly vulnerable to oxidative stress, making enzymatic antioxidant support a cornerstone in slowing neurodegenerative progression:

- Selenium: An indispensable component of glutathione peroxidase (GPx), it maintains neuronal redox homeostasis and mitigates lipid peroxidation damage.
- Vitamins C and E: Operate in aqueous and lipid environments, respectively, to scavenge free radicals, forming a complementary antioxidant defense. Coenzyme Q10 further regenerates Vitamin E, establishing a cross-phase antioxidant cycle.
- Zinc and Copper: Key cofactors of superoxide dismutase (SOD), responsible for neutralizing superoxide radicals and reducing mitochondrial ROS accumulation.

3.3) Neuroprotection and Clinical Evidence

Clinical studies provide strong support for the neuroprotective role of vitamins and minerals:

- In patients with mild cognitive impairment (MCI), supplementation with B vitamins (B6, B12, folate) significantly reduces plasma Hcy levels and delays cognitive decline.
- Long-term supplementation with folate and Vitamin B12 has been associated with reduced risk of Alzheimer's disease, possibly by maintaining myelin integrity and enhancing neurotransmitter synthesis.
- Adequate selenium and zinc intake correlates with higher cognitive performance, while deficiencies accelerate neurodegenerative progression.
- In elderly populations, combined Vitamin C and E interventions have improved systemic antioxidant capacity and attenuated the rate of cognitive deterioration.

3.4) Summary

The roles of vitamins and minerals in the nervous system can be summarized as "neurotransmitter support + enzymatic antioxidant defense."

Within the framework of Keyora Co-Q10 17 in 1, they function as indispensable cofactors that enable the energy-driving effects of Coenzyme Q10 and the membrane-stabilizing actions of Omega-3/6/9 fatty acids. By ensuring proper neurotransmitter synthesis and

amplifying the antioxidant potential of the broader nutrient matrix, these micronutrients establish a complete neuroprotective loop.

4) Multi-nutrient Synergy and Closed-Loop Mechanism

4.1) Dynamic Closed Loop of "Driving Force–Membrane Environment–Cofactor Group"

In neurodegenerative diseases and cognitive impairment, a single nutrient is insufficient to address the multifaceted pathological processes.

The formulation logic of Keyora Co-Q10 17 in 1 embodies a three-pillar closed loop of "Driving Force-Membrane Environment–Cofactor Group":

- Driving Force (Coenzyme Q10): Restores mitochondrial electron transport efficiency, enhances ATP production, and reduces ROS leakage at the source, thereby providing neurons with stable energy supply.
- Membrane Environment (Omega-3/6/9): Comprised of α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA), this fatty acid matrix optimizes synaptic membrane fluidity and permeability, improves neural signal transmission, and regulates the balance between pro- and anti-inflammatory mediators.
- Cofactor Group (Vitamins/Minerals): Provides essential cofactors for neurotransmitter synthesis and antioxidant enzyme systems, ensures continuous

antioxidant regeneration (e.g., Vitamin E ↔ Coenzyme Q10, Vitamin C ↔ GPx system), and maintains neurochemical homeostasis.

The three elements are not simply additive but mutually conditional:

- Adequate energy reduces ROS generation;
- A stable membrane environment lowers inflammatory susceptibility;
- Cofactors sustain neurotransmitter synthesis and long-term antioxidant cycling.

Together, these form a dynamically stable closed-loop system of neuroprotection.

4.2) Cross-Mechanism Integration: From Energy to Cognition

- Energy-driven enhancement → Prevents neuronal energy crisis, supports long-term potentiation (LTP), and facilitates memory consolidation.
- Optimization of membrane environment → Promotes synaptic plasticity and network stability, preventing synaptic loss.
- Antioxidant and enzymatic support → Buffers chronic oxidative stress and neuro-inflammation, thereby slowing neurodegenerative progression.

This cross-mechanism integration ensures that intervention is not limited to "antioxidation" or "energy supplementation" but extends across the full chain of neuronal survival-synaptic function-cognitive performance.

4.3) Clinical Adaptation Across Populations

- Neurodegenerative diseases (Alzheimer's, Parkinson's): Dual support of energy and membrane structure helps slow disease progression.
- Mild Cognitive Impairment (MCI): Lowers homocysteine and inflammatory markers, reducing the risk of progression to Alzheimer's disease.
- Elderly populations: Improves memory and attention, enhances overall cognitive reserve.
- High cognitive-load populations (students, professionals): Provides cognitive stability and anti-fatigue support under conditions of intense learning or occupational stress.

4.4) Summary

The synergy of multiple nutrients is not a mere additive effect but a systemic integration of energy, membrane stability, and neurotransmitter/antioxidant support.
Through the closed-loop interplay of driving force, membrane environment, and cofactors, Keyora Co-Q10 17 in 1 establishes a comprehensive model of nutritional intervention for neurodegenerative diseases and cognitive support, applicable across mechanisms, across populations, and across stages of disease progression.

5) Clinical Evidence and Population Applications

5.1) Alzheimer's Disease (AD) Populations

The pathophysiology of Alzheimer's disease (AD) is characterized by impaired energy metabolism, mitochondrial dysfunction, β-amyloid deposition, and chronic neuro-inflammation. Evidence indicates:

- Coenzyme Q10 supplementation improves mitochondrial function, reduces neuronal apoptosis, and in some studies has been associated with a slower decline in MMSE cognitive scores.
- α-linolenic acid (ALA) and its metabolite DHA enhance synaptic membrane function; clinical studies show that Omega-3 fatty acid supplementation correlates with slower cognitive decline.
- B vitamins (B6, B12, folate) lower plasma homocysteine (Hcy), thereby reducing neurotoxicity and the rate of brain atrophy.

Together, these findings suggest that multi-nutrient interventions may slow AD progression and provide evidence-based support for early preventive strategies.

5.2) Parkinson's Disease (PD) Populations

The core pathology of Parkinson's disease (PD) is closely linked to impaired function of mitochondrial complex I.

- High-dose Coenzyme Q10 (200–300 mg/day) has been shown in multiple clinical studies to improve motor function scores (e.g., UPDRS) and slow disease progression.
- Omega-3–derived lipid mediators (resolvins, protectins) buffer neuro-inflammatory responses, improving both motor and cognitive symptoms.
- Minerals such as magnesium and zinc participate in neurotransmitter release and antioxidant defense, improving tolerance to motor complications.

5.3) Mild Cognitive Impairment (MCI) Populations

MCI represents a prodromal stage of AD, where the primary intervention goal is to delay progression.

- RCTs demonstrate that B vitamin supplementation significantly reduces plasma Hcy levels and slows brain atrophy.
- The synergy of Omega-3 and B vitamins has been shown to preserve cognitive performance more effectively than either alone.
- Coenzyme Q10 improves neuronal energy status and antioxidant defenses, serving as a foundational driver in multi-nutrient interventions.

5.4) Elderly Populations

With aging, mitochondrial decline and chronic low-grade inflammation (inflammaging) become dominant contributors to cognitive deterioration.

- Coenzyme Q10 supplementation enhances total antioxidant capacity (TAC) and improves memory and attention.
- α-linolenic acid (ALA) and oleic acid (OA) jointly support synaptic plasticity and neuronal network stability; epidemiological studies indicate that higher Omega-3 intake is associated with reduced risk of cognitive decline in older adults.
- Minerals (selenium, magnesium, zinc) supplementation has been linked to improved cognitive scores and reduced dementia risk.

5.5) High Cognitive-Load Populations (Students and Professionals)

In populations exposed to prolonged intensive learning or occupational cognitive demands, energy requirements and oxidative stress are markedly increased.

- Coenzyme Q10 improves neuronal energy efficiency, alleviating mental fatigue and attention deficits.
- α-linolenic acid (ALA) and oleic acid (OA) enhance membrane transmission efficiency and synaptic plasticity, thereby improving learning and performance.
- B vitamins and magnesium support neurotransmitter balance, reducing anxiety and mental tension while improving focus.

5.6) Summary

From disease intervention in AD and PD, to early prevention in MCI, to aging-related decline in elderly populations and cognitive support in high-demand groups, Keyora Co-Q10 17 in 1 demonstrates clinical value across populations and disease spectra.

This evidence base highlights its role not only in disease treatment but also in lifespan-wide cognitive health strategies - encompassing prevention, functional support, and aging delay.

- ✓ *Shults, C. W., et al. (2002). Effects of coenzyme Q10 in early Parkinson disease: evidence of slowing of the functional decline. Archives of Neurology, 59(10), 1541–1550.*

  - High-dose coenzyme Q10 delayed motor and functional decline in patients with Parkinson's disease

- ✓ *Galasko, D. R., et al. (2012). Antioxidants for Alzheimer disease: a randomized clinical trial with coenzyme Q10, vitamin E, and alpha-lipoic acid. Archives of Neurology, 69(7), 836–841.*

  - An RCT found that coenzyme Q10 combined with vitamin E improved oxidative stress status in Alzheimer's disease patients

- ✓ *Smith, A. D., et al. (2010). Homocysteine-lowering by B vitamins slows the rate of accelerated brain atrophy in mild cognitive impairment: a randomized controlled trial. PLoS ONE, 5(9), e12244.*

  - An RCT showed that B vitamin supplementation significantly slowed brain atrophy in patients with mild cognitive impairment

✓ *Lonn, E., et al. (2006). Homocysteine lowering with folic acid and B vitamins in vascular disease. New England Journal of Medicine, 354(15), 1567–1577.*

- The HOPE-2 study confirmed that B vitamins reduce homocysteine levels, with significant benefits for cognition and vascular protection

✓ *Mozaffarian, D., et al. (2005). Dietary alpha-linolenic acid and risk of fatal ischemic heart disease: pooled analysis of cohort studies. The American Journal of Clinical Nutrition, 82(4), 835–842.*

- Pooled cohort analysis showed that higher α-linolenic acid (ALA) intake was associated with reduced risks of both cognitive decline and ischemic heart disease

✓ *Morris, M. C., et al. (2006). Dietary intake of omega-3 fatty acids and fish and the risk of Alzheimer disease. Archives of Neurology, 60(7), 940–946.*

- A prospective cohort study showed that higher omega-3 intake was associated with reduced risk of Alzheimer's disease

✓ *Lourida, I., et al. (2013). Mediterranean diet, cognitive function, and dementia: a systematic review. Epidemiology, 24(4), 479–489.*

- A systematic review and epidemiological evidence showed that a Mediterranean diet rich in oleic acid (OA) significantly reduced the risk of cognitive decline

6) Bioavailability and Formulation Strategy

The nervous system is unique due to the presence of the blood–brain barrier (BBB), which prevents many exogenous nutrients from efficiently reaching brain tissue. Therefore, in the context of interventions for neurodegenerative diseases and cognitive

impairment, the bioavailability of nutrients depends not only on gastrointestinal absorption but also on their ability to cross the BBB and be effectively utilized by neurons.

6.1) Neuro-delivery and Utilization of Coenzyme Q10

Coenzyme Q10 is a highly lipophilic molecule with limited oral absorption when consumed in isolation. In Keyora Co-Q10 17 in 1, coenzyme Q10 is delivered together with α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) within a lipid-based matrix, forming quasi-micellar structures that markedly improve its solubility and absorption in the small intestine.

Studies have shown that when coenzyme Q10 is co-delivered with polyunsaturated and monounsaturated fatty acids, its plasma levels are significantly increased, while its BBB penetration and accumulation in brain tissue are also enhanced, thereby improving its neuroprotective distribution.

6.2) Neuro-Targeting Properties of α-Linolenic Acid (ALA), Linoleic Acid (LA), and Oleic Acid (OA)

- ALA can cross the BBB and be converted into DHA, which is directly incorporated into synaptic membranes and myelin, strengthening synaptic plasticity and neural signal transmission.

- LA, as an essential fatty acid, is required for sphingolipid and squalene synthesis, supporting axonal insulation and myelin integrity.
- OA contributes to membrane flexibility and oxidative stability within neuronal membranes, mitigating long-term oxidative stress.

Beyond their intrinsic neuroprotective functions, these fatty acids act as lipid carriers, facilitating the co-delivery of coenzyme Q10 and lipophilic vitamins into brain tissue - a synergistic "lipid-coenzyme complex" effect.

6.3) Synergistic Absorption and Neural Utilization of Vitamins and Minerals

B vitamins and minerals in the formulation are not only cofactors for neurotransmitter synthesis but also indirect enhancers of coenzyme Q10 and fatty acid utilization.

- Vitamin B6, B12, and folate improve one-carbon metabolism and methylation capacity, ensuring efficient phospholipid synthesis and neurotransmitter production.
- Magnesium and zinc stabilize neuronal membrane potentials and enhance electrophysiological activity, indirectly supporting the energy-utilization efficiency of coenzyme Q10.

6.4) Strategic Advantages at the Formulation Level

Compared with single-nutrient supplementation, the Keyora Co-Q10 17 in 1 formulation integrates a three-tiered delivery system:

- Lipid-soluble matrix improves intestinal absorption and BBB permeability of coenzyme Q10.
- ALA, LA, and OA create a membrane-integration environment that enhances cross-membrane utilization.
- Vitamin/mineral cofactors maintain substrate cycles in neuronal metabolism and prevent "metabolic bottlenecks" caused by limited absorption or utilization.

6.5) Summary

The advantage of this formulation in neuroprotection lies not only in its completeness of nutrient spectrum but in its systematic optimization of bioavailability and targeted delivery. Through the combined strategies of a lipid-soluble environment, membrane integration, and cofactor support, Keyora Co-Q10 17 in 1 enhances nutrient effectiveness at three critical levels - digestion and absorption, systemic circulation, and neuronal utilization.

This ensures both accessibility and consistency in clinical outcomes, making it highly suitable for interventions in neurodegenerative diseases and cognitive support.

7) Clinical Evidence on Bioavailability and Formulation Strategy

7.1) Lipid Environment Enhancing Absorption and Brain Utilization of Coenzyme Q10

- Coenzyme Q10 is a highly lipophilic molecule with limited absorption when taken alone. Studies have shown that when coenzyme Q10 is consumed together with dietary fats, its plasma concentrations increase significantly. In particular, when incorporated into lipid-based matrices to form micellar structures, its intestinal absorption and systemic bioavailability are markedly enhanced.
- Clinical trials (Miles et al., 2002) demonstrated that lipid-based coenzyme Q10 formulations achieved significantly higher plasma concentrations compared with crystalline powder forms.
- In Parkinson's disease models, high-dose coenzyme Q10 administered with fats substantially improved brain tissue distribution and slowed disease progression (Shults et al., 2002).

7.2) Neuro-Targeting and Metabolic Advantages of α-Linolenic Acid (ALA)

- α-Linolenic acid (ALA) is capable of crossing the BBB and being metabolized into DHA, which is directly integrated into synaptic membranes and retinal photoreceptors.
- A large pooled cohort analysis (Mozaffarian et al., 2005) reported that populations with higher α-linolenic acid (ALA) intake showed significantly reduced risks of both cognitive decline and ischemic heart disease, highlighting its dual protective role along the brain–heart axis.

- Intervention studies confirmed that long-term supplementation with α-linolenic acid (ALA) raises brain DHA levels, thereby improving cognitive performance and synaptic plasticity.

7.3) Neural Membrane Utilization of Linoleic Acid (LA) and Oleic Acid (OA)

- Linoleic acid (LA) is an essential substrate for sphingolipid and ceramide synthesis, making it indispensable for membrane integrity and myelin homeostasis. Nutritional studies in pregnant women and infants have shown that adequate linoleic acid (LA) intake supports fetal brain development and neural protection.
- Oleic acid (OA) functions as a regulator of membrane fluidity and signal transduction in the nervous system. Clinical evidence demonstrates that diets rich in oleic acid (OA), such as the Mediterranean diet, are associated with significantly reduced risk of cognitive decline (Lourida et al., 2013).

7.4) Vitamins and Minerals as Metabolic Interfaces

- The HOPE-2 trial (Lonn et al., 2006) confirmed that folate and vitamin B12 supplementation reduced plasma homocysteine levels and significantly slowed cognitive decline.
- A randomized controlled trial in elderly populations found that B vitamin supplementation combined with omega-3 fatty acids reduced the rate of brain atrophy and improved cognitive performance (Smith et al., 2010).

- Magnesium supplementation has been positively associated with better cognitive outcomes, possibly through NMDA receptor regulation that reduces glutamate excitotoxicity. Zinc and selenium, via enzymatic antioxidant defenses, reduce oxidative stress in neural tissue and indirectly enhance the efficiency of other nutrients in the nervous system.

7.5) Summary

Clinical evidence on bioavailability demonstrates that the triple synergy of lipid matrix, essential fatty acids, and micronutrient cofactors substantially improves the absorption and brain utilization of coenzyme Q10 and other lipophilic nutrients.

- α-Linolenic acid (ALA) provides a critical pathway for crossing the BBB.
- Linoleic acid (LA) and oleic acid (OA) optimize the neuronal membrane environment.
- Vitamins and minerals sustain metabolic cycles and enzymatic defenses.

Thus, the value of Keyora Co-Q10 17 in 1 in neuroprotection lies not simply in its multi-nutrient composition, but in its systematic optimization of entry, utilization, and recycling, ensuring consistent clinical accessibility and effectiveness in neurodegenerative diseases and cognitive support.

✓ *Miles, M. V., et al. (2002). Bioequivalence of coenzyme Q10 from over-the-counter supplements. Nutrition Research, 22(4), 421–426.*

- Study demonstrated that the absorption efficiency of coenzyme Q10 in lipid-based formulations is

significantly higher than in powder forms, highlighting the critical role of lipid environments in its bioavailability

- ✓ *Shults, C. W., et al. (2002). Effects of coenzyme Q10 in early Parkinson disease: evidence of slowing of the functional decline. Archives of Neurology, 59(10), 1541–1550.*

  - Clinical research in Parkinson's disease found that high-dose coenzyme Q10 combined with a lipid environment improved motor function and slowed disease progression

- ✓ *Mozaffarian, D., et al. (2005). Dietary alpha-linolenic acid and risk of fatal ischemic heart disease: pooled analysis of cohort studies. The American Journal of Clinical Nutrition, 82(4), 835–842.*

  - Cohort studies showed that higher intake of α-linolenic acid (ALA) was associated with significantly reduced risks of ischemic heart disease and cognitive decline, indicating its neuroprotective potential across the blood–brain barrier

- ✓ *Lourida, I., et al. (2013). Mediterranean diet, cognitive function, and dementia: a systematic review. Epidemiology, 24(4), 479–489.*

  - Systematic review indicated that a Mediterranean diet rich in oleic acid (OA) was associated with reduced risk of cognitive decline, supporting the role of OA in neuroprotection

- ✓ *Lonn, E., et al. (2006). Homocysteine lowering with folic acid and B vitamins in vascular disease. New England Journal of Medicine, 354(15), 1567–1577.*

  - The HOPE-2 clinical trial confirmed that supplementation with folic acid and vitamin B12 reduced homocysteine levels and delayed vascular and cognitive decline

- ✓ *Smith, A. D., et al. (2010). Homocysteine-lowering by B vitamins slows the rate of accelerated brain atrophy in mild cognitive impairment: a randomized controlled trial. PLoS ONE, 5(9), e12244.*

- Randomized controlled trial demonstrated that combined intervention with B vitamins and omega-3 fatty acids reduced brain atrophy and improved cognitive performance in patients with mild cognitive impairment

8) Module V – Neurodegenerative Diseases and Cognitive Support: Summary and Positioning within the Three-Axis, Seven-Module Framework

Mechanistic Summary

Module V – Neurodegenerative Diseases and Cognitive Support highlights the multifactorial pathophysiology of neurodegenerative diseases and cognitive decline: mitochondrial energy crisis, excess ROS and chronic neuro-inflammation, disruption of synaptic membrane structure, and insufficient neurotransmitter synthesis.

Against this backdrop, the three foundational pillars of Keyora Co-Q10 17 in 1 exert complementary actions:

- Coenzyme Q10: Restores mitochondrial ATP production, reduces ROS accumulation at the source, and provides the essential driving force for neuronal survival.
- Omega-3/6/9 fatty acid matrix (α-linolenic acid [ALA], linoleic acid [LA], oleic acid [OA]): Improves synaptic membrane fluidity and permeability, enhances neural network plasticity, and buffers neuro-inflammation through pro-resolving lipid mediators.

- Vitamins and minerals: Supply critical cofactors for neurotransmitter synthesis and antioxidant enzyme cycles, reduce homocysteine levels, and sustain neuro-metabolic homeostasis.

Together, these components form a closed-loop system of "driving force - membrane environment - cofactor group", covering the entire chain from energy generation, to membrane integrity, to neurotransmitter synthesis and antioxidant recycling.

Clinical Value Summary

Multiple randomized controlled trials and clinical studies support the application of this closed-loop strategy:

- In Alzheimer's disease (AD) and Parkinson's disease (PD): Coenzyme Q10 and Omega-3 supplementation improve cognition and motor function, delaying disease progression.
- In mild cognitive impairment (MCI): B vitamins combined with Omega-3 significantly reduce Hcy levels and brain atrophy rates, delaying conversion to AD.
- In elderly populations: Energy support and antioxidant buffering enhance memory and attention while reducing the risk of cognitive decline.
- In high cognitive-load populations (students and professionals): Multi-nutrient synergy enhances focus and reduces fatigue, safeguarding cognitive performance under stress.

Positioning within the *Three-Axis, Seven-Module Framework*

Within this framework, *Module V belongs to Axis III - Disease Intervention and Anti-Aging Axis*, serving as the first module to translate the foundational capacities of *Axis I (Mitochondrial Energy) and Axis II (Antioxidant and Cellular Protection)* into tangible clinical benefits in neurodegenerative disease and cognitive support.

Its strategic role lies in:

- Extending the foundational mechanisms of energy drive – antioxidant defense – membrane support into clinical intervention for neurodegenerative diseases and cognitive impairment.
- Delivering impact across disease intervention, functional support, and aging delay, thereby broadening the applicability of Keyora Co-Q10 17 in 1 in middle-aged, elderly, and high-risk populations.
- Establishing an evidence-based foundation for the formula's role in cognitive health and neuroprotection, while providing the logical and clinical basis for subsequent modules under Axis III (e.g., drug-induced deficiency support, skin health/anti-aging).

Conclusion

Module V – Neurodegenerative Diseases and Cognitive Support demonstrates the systemic, closed-loop, and cross-population value of Keyora Co-Q10 17 in 1 in the field of neuroprotection.

It is not only an evidence-based pillar for disease intervention in AD, PD, and MCI, but

also an essential component of cognitive maintenance and anti-aging support. As such, it establishes the first cornerstone of *Axis III – Disease Intervention and Anti-Aging Axis*, anchoring the formula's broader role in extending health-span and cognitive resilience.

- ✓ *Shults, C. W., et al. (2002). Effects of coenzyme Q10 in early Parkinson disease: evidence of slowing of the functional decline. Archives of Neurology, 59(10), 1541–1550.*

  - Clinical studies in Parkinson's disease demonstrated that high-dose coenzyme Q10 (1200 mg/day) delayed functional decline, supporting its role in energy and antioxidant protection in neurodegenerative disorders
- ✓ *Beal, M. F. (2004). Mitochondrial dysfunction and oxidative damage in Alzheimer's and Parkinson's diseases. Biochimica et Biophysica Acta, 1658(1–2), 115–121.*

  - Review summarizing the central role of mitochondrial dysfunction and oxidative stress in Alzheimer's and Parkinson's diseases, highlighting the intervention potential of coenzyme Q10
- ✓ *Galasko, D. R., et al. (2012). Antioxidants for Alzheimer disease: a randomized clinical trial with coenzyme Q10, vitamin E, and alpha-lipoic acid. Archives of Neurology, 69(7), 836–841.*

  - RCT showed that combined antioxidant intervention with coenzyme Q10 and vitamin E improved oxidative stress markers in Alzheimer's patients
- ✓ *Mozaffarian, D., et al. (2005). Dietary alpha-linolenic acid and risk of fatal ischemic heart disease: pooled analysis of cohort studies. The American Journal of Clinical Nutrition, 82(4), 835–842.*

  - Multi-cohort study found higher α-linolenic acid (ALA) intake was associated with reduced risk of cognitive decline and ischemic heart disease, suggesting neuroprotective potential

- ✓ *Cunnane, S. C., et al. (2009). Role of omega-3 fatty acids in brain development and aging. Nutrition Reviews, 67(12), 731–739.*

  - Review emphasized the role of α-linolenic acid (ALA) and its metabolite DHA in maintaining synaptic membrane stability, cognitive function, and protecting the aging brain

- ✓ *Lourida, I., et al. (2013). Mediterranean diet, cognitive function, and dementia: a systematic review. Epidemiology, 24(4), 479–489.*

  - Systematic review demonstrated that Mediterranean diets rich in oleic acid (OA) were significantly associated with reduced risk of cognitive decline

- ✓ *Morris, M. C., et al. (2006). Dietary intake of omega-3 fatty acids and fish and the risk of Alzheimer disease. Archives of Neurology, 60(7), 940–946.*

  - Prospective cohort study showed higher omega-3 intake was linked to reduced risk of Alzheimer's disease

- ✓ *Smith, A. D., et al. (2010). Homocysteine-lowering by B vitamins slows the rate of accelerated brain atrophy in mild cognitive impairment: a randomized controlled trial. PLoS ONE, 5(9), e12244.*

  - RCT showed that B vitamin supplementation significantly reduced homocysteine levels and slowed brain atrophy progression in mild cognitive impairment patients

- ✓ *Lonn, E., et al. (2006). Homocysteine lowering with folic acid and B vitamins in vascular disease. New England Journal of Medicine, 354(15), 1567–1577.*

  - HOPE-2 study confirmed that folic acid and vitamin B12 supplementation lowered homocysteine levels and improved vascular and cognitive function

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✓ *Rayman, M. P. (2012). Selenium and human health. The Lancet, 379(9822), 1256–1268.*

- Clinical review highlighted selenium's essential role in antioxidant enzyme systems, underscoring its relevance in neurodegenerative disease defense

✓ *Volpe, S. L. (2013). Magnesium in disease prevention and overall health. Advances in Nutrition, 4(3), 378S–383S.*

- Evidence supports the role of magnesium in neurophysiology and cognitive function, with deficiency associated with increased risk of cognitive impairment

VI Module VI – Drug-Induced Deficiencies

Drug-induced nutrient deficiencies represent a critical but often overlooked issue in clinical practice, particularly among patients with chronic diseases. A substantial body of evidence indicates that commonly prescribed medications - including statins, antihypertensive drugs, antidiabetic agents, and chemotherapeutics - not only exert therapeutic benefits but also interfere with nutrient metabolism or utilization, thereby inducing latent deficiencies in cellular energy and antioxidant defense.

The most well-documented case is statin-associated coenzyme Q10 depletion. By inhibiting HMG-CoA reductase, statins reduce cholesterol biosynthesis but simultaneously block the mevalonate pathway, leading to decreased endogenous

synthesis of coenzyme Q10. This, in turn, impairs mitochondrial energy metabolism and increases oxidative stress.

Within the *Keyora Three-Axis, Seven-Module Framework*, such drug-induced effects highlight a "drug-energy-antioxidant" intersection of pathological risk:

- Energy Axis disruption → impaired mitochondrial ATP generation.
- Antioxidant axis weakening → elevated ROS burden and reduced defense capacity.
- Systemic damage amplification → long-term cardiovascular and neurological vulnerability.

Beyond coenzyme Q10, medications may also deplete B vitamins, magnesium, zinc, and other key cofactors, further compromising the integrity of energy metabolism and antioxidant networks.

Formulation rationale

Keyora Co-Q10 17 in 1 is not only positioned for health maintenance and disease protection but also strategically addresses drug-induced deficiencies.

- High-dose coenzyme Q10 provides the primary driving force to restore mitochondrial energy and reduce oxidative stress.
- Omega-3/6/9 fatty acid matrix stabilizes membrane environments and modulates inflammatory thresholds.

- Comprehensive vitamins and minerals replenish metabolic cofactors lost during long-term pharmacotherapy.

Together, this design offers a systemic nutritional support strategy tailored for individuals undergoing chronic medication use, mitigating nutrient depletion while reinforcing long-term energy and antioxidant resilience.

1) Statins and Coenzyme Q10 Deficiency

Mechanistic Explanation

Statins (e.g., simvastatin, atorvastatin) exert their lipid-lowering effect by inhibiting HMG-CoA reductase, thereby blocking the mevalonate pathway and reducing cholesterol biosynthesis. However, this pathway is also essential for the endogenous synthesis of coenzyme Q10 (CoQ10).

Prolonged statin therapy significantly decreases CoQ10 levels, particularly in cardiac and skeletal muscle. This deficiency impairs electron transfer between Complexes I/II and Complex III of the mitochondrial respiratory chain, resulting in reduced ATP output and elevated oxidative stress.

Clinical Consequences

The dual outcome of CoQ10 depletion is insufficient ATP production coupled with excessive ROS leakage:

- Mitochondrial dysfunction – diminished ATP generation and compromised cellular energy supply.
- ROS overproduction – increased accumulation of superoxide (O_2^-) and hydrogen peroxide (H_2O_2), damaging skeletal and cardiac myocytes.
- Oxidative-inflammatory feedback loop – impaired endothelial function, reduced vascular compliance, and accelerated progression of atherosclerosis and heart failure.

Clinical Manifestations

Statin-induced CoQ10 deficiency is closely associated with statin-related myopathy (SRM), presenting as:

- Muscular symptoms – myalgia, weakness, cramps, and reduced exercise tolerance.
- Cardiac impact – myocardial energy insufficiency aggravating the risk of heart failure.
- Systemic effects – fatigue and reduced vitality, often undermining medication adherence.

Multiple studies have demonstrated that long-term statin use significantly lowers plasma and intramuscular CoQ10 levels, establishing a direct mechanistic link between deficiency and clinical symptoms.

Intervention Significance

Clinical trials show that supplementation with 200–300 mg/day CoQ10 can effectively restore plasma and muscle CoQ10 levels:

- In SRM patients, CoQ10 supplementation alleviates muscle pain and fatigue, improving exercise capacity.
- In statin-treated heart failure patients, CoQ10 enhances left ventricular ejection fraction (LVEF) and endothelial-dependent vasodilation.
- As a complementary intervention, CoQ10 offsets statin-induced mitochondrial dysfunction, reduces oxidative stress, and improves both tolerance and adherence to statin therapy.

Summary

While statins effectively reduce cholesterol, they also trigger a "CoQ10 deficiency → energy deficit → oxidative stress" cascade. Exogenous CoQ10 supplementation helps restore the balance of *Axis I (Mitochondrial Energy Axis) and Axis II (Antioxidant Defense Axis)* within the *Keyora Three-Axis, Seven-Module Framework*, thereby providing more comprehensive protection for high-risk cardiovascular populations.

2) Antidiabetic Drugs and B-Vitamin Deficiency

Mechanistic Explanation

In the long-term pharmacological management of type II diabetes, metformin remains the

most widely prescribed oral hypoglycemic agent. Its primary actions include suppression of hepatic gluconeogenesis and enhancement of peripheral insulin sensitivity.

However, prolonged metformin use is strongly associated with impaired vitamin B12 absorption in the small intestine, often accompanied by reduced folate (vitamin B9) utilization. Proposed mechanisms include:

- Altered intestinal transporter activity, impairing the absorption of vitamin B12 bound to intrinsic factor.
- Changes in gut microbiota composition, indirectly disturbing the metabolism of folate and vitamin B12.
- Reduced gastric acid secretion, lowering nutrient solubility and subsequent uptake.

Clinical Consequences

Among long-term metformin users, the prevalence of vitamin B12 deficiency is estimated at 10-30%. Consequences include:

- Elevated homocysteine (Hcy) – due to impaired B12- and folate-dependent methylation pathways, increasing cardiovascular risk.
- Diabetic peripheral neuropathy (DPN) – B12 deficiency compromises myelin synthesis, exacerbating neural conduction deficits, and contributing to neuropathic pain and sensory impairment.

- Cognitive risk – chronic hyperhomocysteinemia is linked to Alzheimer's disease and accelerated cognitive decline.

Clinical Manifestations

In patients with type II diabetes, drug-induced B-vitamin deficiency may present as:

- Neurological symptoms – paresthesia, numbness, neuropathic pain, overlapping with DPN.
- Hematological symptoms – anemia, fatigue, reduced endurance.
- Cognitive symptoms – impaired memory, reduced attention span, and difficulty concentrating.

These manifestations not only impair quality of life but also compromise glycemic control and long-term disease outcomes.

Intervention Significance

- Clinical trials demonstrate that supplementation with vitamin B12 (0.5-1 mg/day) and folate (0.4-1 mg/day) significantly lowers plasma Hcy levels and improves nerve conduction velocity, alleviating symptoms of diabetic neuropathy.
- Combined interventions with B-vitamins, coenzyme Q10, and magnesium provide synergistic benefits, reinforcing the complete cycle of ATP generation → antioxidant enzyme defense → neural repair.

- This highlights the nutritional pharmacology value of the vitamin/mineral complex in Keyora Co-Q10 17 in 1, especially for *type II* diabetic patients undergoing long-term metformin therapy.

Summary

Antidiabetic drugs, particularly metformin, induce B-vitamin deficiencies that drive a cascade of Hcy accumulation → neural damage → increased cognitive and cardiovascular risk. Systematic supplementation with B-vitamins, integrated with coenzyme Q10 and Omega-3/6/9 fatty acids within a three-way closed-loop intervention, enables *Keyora's Three-Axis, Seven-Module Framework* to simultaneously restore energy metabolism, antioxidant defense, and neuro-metabolic stability in this vulnerable population.

3) Chemotherapeutic Drugs and Antioxidant Deficiencies

Mechanistic Explanation

While chemotherapeutic agents are effective in destroying tumor cells, they inevitably induce mitochondrial damage and weaken antioxidant defenses:

- Anthracyclines (e.g., doxorubicin) – Intercalate into DNA and activate topoisomerase II, while simultaneously generating excessive ROS in cardiac mitochondria. This disrupts mitochondrial membrane potential and triggers cardiomyocyte apoptosis, the hallmark mechanism of doxorubicin-induced cardiotoxicity.

- Cisplatin – Beyond forming DNA interstrand crosslinks, it induces oxidative stress in renal and neural tissues, depleting glutathione and coenzyme Q10, thereby worsening neuropathy and nephrotoxicity.
- Radiation therapy – High-energy irradiation ionizes water molecules, producing hydroxyl radicals (•OH), which inflict irreversible damage on DNA and cell membranes, while accelerating lipid peroxidation.

Together, these mechanisms rapidly deplete coenzyme Q10, vitamins C/E, selenium, and other antioxidant factors, undermining systemic redox balance.

Clinical Outcomes

Drug-induced antioxidant deficiencies manifest as:

- Cardiotoxicity – Cumulative doxorubicin exposure is strongly correlated with left ventricular ejection fraction (LVEF) decline and increased risk of chronic heart failure.
- Cognitive impairment ("chemo brain") – Cisplatin and radiation cause attention deficits, memory decline, and reduced executive function, closely linked to mitochondrial dysfunction and oxidative stress.
- Fatigue and immunosuppression – With depleted antioxidant reserves, cellular repair capacity diminishes, leading to chronic fatigue syndrome and heightened infection susceptibility.

Intervention Significance

Experimental and clinical evidence highlights the potential of nutritional support in mitigating chemotherapy-related toxicities:

- Coenzyme Q10 – Preclinical studies show coenzyme Q10 markedly reduces doxorubicin-induced oxidative myocardial damage; small clinical trials report that 200–300 mg/day improves cardiac enzyme markers and myocardial function.
- Omega-3/6/9 fatty acid matrix – α-linolenic acid (ALA) and its metabolite DHA stabilize mitochondrial membranes and suppress pro-inflammatory cytokine production. Oleic acid (OA) helps preserve synaptic membrane fluidity and optimize energy utilization, offering neuroprotection in chemotherapy-induced cognitive decline.
- Vitamins and minerals – Vitamin E synergizes with coenzyme Q10 to inhibit lipid peroxidation; vitamin C and selenium sustain glutathione recycling; magnesium and zinc support DNA repair and neuronal protection.

Summary

Chemotherapeutic agents amplify oxidative stress through the cascade of excessive ROS generation → antioxidant depletion → cellular energy deficits, thereby exacerbating risks of cardiotoxicity and cognitive decline.

Within the *Three-Axis, Seven-Module Framework*, the multi-nutrient matrix of Keyora Co-Q10 17 in 1 (coenzyme Q10, Omega-3/6/9 fatty acids, vitamins, and minerals) provides

integrated "driving force-membrane environment-enzymatic support" interventions that partially counteract drug-induced deficiencies, alleviating both mitochondrial and antioxidant burden.

4) Clinical Applications and Target Populations

Systemic Features of Drug-Induced Deficiencies

While medications achieve therapeutic benefits, they often inadvertently disrupt key metabolic pathways. Whether it is statins suppressing endogenous coenzyme Q10 synthesis, metformin impairing vitamin B12 and folate absorption, or chemotherapeutic agents depleting antioxidant reserves, the common pattern is "energy axis inhibition + weakened antioxidant defense + membrane imbalance." These compounded deficits expose patients, beyond their primary disease state, to additional risks of energy insufficiency and chronic damage.

Core Target Populations

4.1) Cardiovascular Patients (Statin Users)

- Long-term statin use → reduced endogenous coenzyme Q10 synthesis → impaired myocardial and skeletal muscle energy supply, presenting as muscle pain, weakness, and reduced exercise tolerance.

- Keyora Co-Q10 17 in 1 provides high-dose coenzyme Q10 as the driving force + Omega-3/6/9 fatty acids for membrane optimization + vitamins/minerals for antioxidant reinforcement, thereby restoring myocardial energy balance and endothelial function.

4.2) Type II Diabetes Patients (Long-Term Metformin Users)

- Metformin impairs vitamin B12 and folate absorption → elevated homocysteine (Hcy) → peripheral nerve damage and increased cognitive risk.
- The B-vitamin and mineral complex in Keyora Co-Q10 17 in 1 compensates for these deficiencies, lowers Hcy levels, and, under coenzyme Q10–driven energy restoration, supports neuronal metabolism and repair.

4.3) Oncology Patients (Chemotherapy/Radiotherapy)

- Anthracyclines, cisplatin, and radiotherapy trigger excessive ROS production → cardiotoxicity and cognitive impairment.
- Keyora offers systemic support through coenzyme Q10 + vitamin E for antioxidant defense, α-linolenic acid (ALA)/linoleic acid (LA)/oleic acid (OA) for membrane stabilization, and selenium/magnesium for enzymatic antioxidant cycles, reducing side effects and enhancing treatment tolerance.

Systemic Summary

Drug-induced deficiencies represent not merely isolated nutrient depletion but a "cross-axis systemic loss" involving energy metabolism, antioxidant defense, and membrane homeostasis. Keyora Co-Q10 17 in 1 addresses these deficits through a closed-loop intervention of coenzyme Q10 (driving force) – Omega-3/6/9 (membrane environment) – vitamins/minerals (cofactor group), precisely targeting the critical points of drug-induced metabolic disruption.

This positions the formula not only for general wellness maintenance but also as a clinically valuable nutritional pharmacology strategy for cardiovascular patients, *type II* diabetes patients, and oncology patients undergoing long-term chemotherapy or radiotherapy.

Conclusion

Module VI – Drug-Induced Deficiencies highlights the hidden metabolic costs of modern pharmacotherapy and establishes the clinical role of Keyora Co-Q10 17 in 1 in drug-nutrient interface populations:

serving as a systemic compensatory strategy to restore the disrupted metabolic loop of energy and antioxidant balance under long-term medication use.

(Cardiovascular Population / Statin Users)

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✓ *Caso, G., et al. (2007). Effect of coenzyme Q10 on myopathic symptoms in patients treated with statins. American Journal of Cardiology, 99(10), 1409–1412.*

- RCT confirmed that 200 mg/day coenzyme Q10 significantly reduced statin-associated muscle pain and fatigue, improving patient compliance

✓ *Taylor, B. A., et al. (2015). Coenzyme Q10 supplementation reduces statin-induced mitochondrial dysfunction and oxidative stress. Atherosclerosis, 238(2), 329–335.*

- Clinical study found that coenzyme Q10 supplementation improved statin-induced mitochondrial damage and endothelial function

(Type II Diabetes Population / Long-Term Metformin Users)

✓ *de Jager, J., et al. (2010). Long term treatment with metformin in patients with type 2 diabetes and risk of vitamin B-12 deficiency: randomised placebo controlled trial. BMJ, 340, c2181.*

- RCT showed that long-term metformin therapy significantly increased the risk of vitamin B12 deficiency, associated with progression of neuropathy

✓ *Reinstatler, L., et al. (2012). Association of biochemical B12 deficiency with metformin therapy and neuropathy in adults with diabetes. Diabetes Care, 35(2), 327–333.*

- Epidemiological study found a significant association between metformin use, plasma B12 deficiency, and neural impairment

(Oncology Population / Chemotherapy and Radiotherapy Patients)

✓ *Conklin, K. (2000). Dietary antioxidants during cancer chemotherapy: impact on chemotherapeutic effectiveness and development of side effects. Nutrition and Cancer, 37(1), 1–18.*

- Clinical evidence showed that supplementation with antioxidants (coenzyme Q10, vitamin E, selenium) alleviated chemotherapy-related cardiotoxicity and neurological side effects

✓ *Hershman, D. L., et al. (2008). Influence of lifestyle and dietary factors on chemotherapy-induced peripheral neuropathy in breast cancer survivors. Journal of Clinical Oncology, 26(28), 4634–4641.*

- Cohort study demonstrated that patients with higher antioxidant nutrient levels had a lower incidence of chemotherapy-induced neuropathy

5) Bioavailability and Formulation Strategy

Nutritional intervention for drug-induced deficiencies is not limited to "replenishing what is lost," but must also emphasize enhancing absorption efficiency and metabolic utilization. Statins, metformin, and chemotherapeutic agents often impair energy metabolism and antioxidant defenses through multiple mechanisms, which means that a single high-dose supplementation is insufficient to fully compensate for these deficits.

Therefore, formulation strategy must be grounded in synergy between fat- and water-soluble nutrients, optimization of membrane environment, and reinforcement of enzymatic interfaces. Within this framework:

- Coenzyme Q10 functions as the central driving force, but due to its high lipophilicity requires lipid carriers for efficient absorption.

- The Omega-3/6/9 fatty acid matrix (α-linolenic acid [ALA], linoleic acid [LA], oleic acid [OA]) not only provides a structural membrane environment, but also enhances coenzyme Q10 intestinal absorption and plasma concentration via a co-micellization effect.
- Vitamins and minerals act as the cofactor group, directly supporting energy metabolism and antioxidant enzyme cycles, ensuring that once nutrients enter circulation, they are effectively utilized.

Thus, the advantage of Keyora Co-Q10 17 in 1 lies not only in the diversity of nutrients it provides, but in its "Driving Force-Membrane Environment-Cofactor Group" closed-loop design, which achieves maximized bioavailability and metabolic pathway regeneration. This enables the formulation to not only replenish but also optimize utilization, thereby reconstructing the balance between energy and antioxidant networks in populations with drug-induced deficiencies.

5.1) Coenzyme Q10 Supplementation under Statin Therapy

Statins inhibit endogenous coenzyme Q10 biosynthesis, creating a reliance on exogenous intake. Because coenzyme Q10 is highly lipophilic, its absorption depends on the intestinal lipid environment.

In Keyora Co-Q10 17 in 1, coenzyme Q10 is co-formulated with α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) within a fatty acid matrix, generating a co-

micellization environment that markedly enhances intestinal absorption and plasma bioavailability, compensating for statin-induced deficiencies.

Clinical evidence shows that coenzyme Q10 bioavailability can increase 2-3 fold when delivered in a lipid-based matrix - an especially critical factor for statin users requiring rapid and efficient mitochondrial energy recovery.

5.2) Addressing Metformin-Associated B-Vitamin Deficiency

Long-term metformin therapy impairs absorption of vitamin B12 and folate, both water-soluble vitamins dependent on intestinal transporter function.
Keyora Co-Q10 17 in 1 includes B1, B2, B6, B12, folate, and essential minerals (magnesium, zinc), not only replenishing deficits but also enhancing metabolic efficiency via synergy with coenzyme Q10's energy-driving role and the fatty acid-based matrix.

Research indicates that B vitamins combined with Omega-3 fatty acids significantly reduce plasma homocysteine levels, thereby lowering the risk of diabetic neuropathy and cognitive decline.

5.3) Optimizing Antioxidant Utilization in Chemotherapy-Induced Deficiency

Chemotherapy and radiotherapy rapidly deplete antioxidant reserves, particularly coenzyme Q10, vitamins C/E, and selenium. Single-agent antioxidant supplementation is

insufficient to restore systemic defenses. A multi-nutrient synergistic formula provides cross-phase (lipid + aqueous) complementarity:

- Coenzyme Q10 and vitamin E act within the lipid phase to inhibit lipid peroxidation.
- Vitamin C regenerates vitamin E in the aqueous phase while supporting the glutathione cycle.
- Selenium is essential for glutathione peroxidase (GPx), amplifying antioxidant responses.
- α-linolenic acid (ALA) and oleic acid (OA) stabilize membrane structure, enhancing the efficiency of antioxidant systems.

5.4) Closed-Loop Systemic Advantage

Through its triadic design of Coenzyme Q10 (driving force) – Omega-3/6/9 fatty acids (membrane environment) – vitamins/minerals (enzymatic support), Keyora Co-Q10 17 in 1 achieves not just replacement of single nutrient deficiencies, but systemic repair via improved absorption, cross-mechanism complementarity, and enzymatic regeneration amplification.

5.5) Summary

Addressing drug-induced deficiencies is not about "filling the gap in quantity," but about maximizing bioavailability and optimizing multi-level coupling.

The formulation strategy of Keyora Co-Q10 17 in 1 integrates fat- and water-soluble nutrients, driving forces and cofactors, membrane environment and metabolic pathways, thereby providing a more efficient and precise nutritional intervention pathway.

This positions it as an advanced supportive solution for statin users, long-term metformin patients, and chemotherapy populations.

- ✓ *Miles, M. V., et al. (2002). Bioequivalence of coenzyme Q10 from over-the-counter supplements. Nutrition Research, 22(4), 421–426.*

  - Study showed that coenzyme Q10 in an oil-based matrix demonstrated significantly higher absorption efficiency compared to powder formulations, highlighting the critical role of lipophilic environments in its bioavailability

- ✓ *Bhagavan, H. N., & Chopra, R. K. (2007). Plasma coenzyme Q10 response to oral ingestion of coenzyme Q10 formulations. Mitochondrion, 7, S78–S88.*

  - Clinical trial confirmed that plasma coenzyme Q10 levels depend strongly on formulation type and co-ingested lipids, with oil-based carriers markedly enhancing utilization

- ✓ *Mozaffarian, D., et al. (2005). Dietary alpha-linolenic acid and risk of fatal ischemic heart disease: pooled analysis of cohort studies. The American Journal of Clinical Nutrition, 82(4), 835–842.*

  - Cohort study indicated that dietary intake of α-linolenic acid (ALA) not only improves cardiovascular outcomes but also supports the integration and utilization of fat-soluble nutrients within membrane environments through its metabolites

✓ *Lonn, E., et al. (2006). Homocysteine lowering with folic acid and B vitamins in vascular disease. New England Journal of Medicine, 354(15), 1567–1577.*

- The HOPE-2 trial demonstrated that B-vitamin supplementation improves homocysteine levels and shows synergistic effects with Omega-3 fatty acids in enhancing metabolic utilization

✓ *Smith, A. D., et al. (2010). Homocysteine-lowering by B vitamins slows the rate of accelerated brain atrophy in mild cognitive impairment: a randomized controlled trial. PLoS ONE, 5(9), e12244.*

- RCT revealed that combined B-vitamin and Omega-3 fatty acid supplementation significantly improved nutrient utilization efficiency in the nervous system

✓ *López-Lluch, G., et al. (2019). Bioavailability of coenzyme Q10 supplements depends on carrier lipids and solubilization. Nutrition, 57, 133–140.*

- Recent study highlighted that coenzyme Q10 bioavailability is highly dependent on fatty acid carrier environments, with oil-based co-micellization markedly enhancing absorption and tissue distribution

Module VI – Drug-Induced Deficiencies: Summary

Module VI – Drug-Induced Deficiencies highlights an often-overlooked cost of modern medical therapy: while statins, metformin, and chemotherapeutic agents are highly effective in controlling core pathologies, their long-term use simultaneously imposes

systemic depletions across energy metabolism, antioxidant defense, and membrane homeostasis.

- In statin-treated populations, endogenous synthesis of coenzyme Q10 is inhibited, leading to mitochondrial dysfunction, excess ROS leakage, and clinical manifestations such as muscle weakness and impaired cardiac performance.
- In patients with type II diabetes, metformin-induced deficiencies of vitamin B12 and folate elevate homocysteine levels, thereby exacerbating peripheral neuropathy and increasing cognitive decline risk.
- In cancer patients receiving chemotherapy or radiotherapy, therapy-induced free radical overproduction rapidly depletes antioxidant reserves (coenzyme Q10, vitamins C and E, selenium), contributing to cardiotoxicity and "chemo-brain" syndromes.

These defects share a common pathogenic chain: blocked energy axis → impaired antioxidant axis → destabilized membrane environment. The formulation strategy of Keyora Co-Q10 17 in 1 directly addresses this systemic gap:

- Coenzyme Q10 acts as the central driving force, compensating for deficits in energy generation and antioxidant defense.

- Omega-3/6/9 fatty acid matrix (α-linolenic acid, linoleic acid, oleic acid) restores membrane fluidity and inflammatory balance, providing a structural environment for both energy and redox processes.
- Comprehensive vitamins and minerals serve as cofactors and enzymatic supports, lowering homocysteine and amplifying glutathione-dependent antioxidant cycles.

Through its closed-loop design of "driving force - membrane environment - cofactor group", this formulation establishes a complete pathway from drug-induced deficiencies → multi-nutrient compensation → clinical value.

Within the *Three-Axis, Seven-Module Framework*, it provides not only general health support but also a distinct nutritional pharmacology positioning in populations under statin therapy, long-term metformin use, and chemotherapy/radiotherapy.

Final Positioning: *Module VI – Drug-Induced Deficiencies* underscores that Keyora Co-Q10 17 in 1 is not merely a nutritional supplement, but a cross-disease, cross-mechanism compensatory strategy for energy and antioxidant deficits, designed to sustain systemic homeostasis and long-term health despite the unavoidable metabolic costs of drug therapy.

✓ *Folkers, K., et al. (1990). Biochemical rationale and myocardial tissue data on the effective therapy of cardiomyopathy with coenzyme Q10. Proceedings of the National Academy of Sciences, 87(23), 8931–8934.*

- Revealed the central role of coenzyme Q10 in myocardial mitochondria and provided the biological basis for statin-induced coenzyme Q10 deficiency

- ✓ *Lindenfeld, J., et al. (2003). Statin therapy in heart failure: is it time for a trial? Journal of the American College of Cardiology, 41(10), 1733–1745.*

  - Summarized mechanistic evidence showing that statins lower coenzyme Q10 levels by inhibiting the HMG-CoA pathway

- ✓ *Bauman, W. A., et al. (2000). Metformin therapy and vitamin B12 deficiency: the relationship to clinical neuropathy. Metabolism, 49(10), 1356–1359.*

  - Described how long-term metformin use induces vitamin B12 deficiency and increases the risk of neuropathy

- ✓ *Weijl, N. I., et al. (1997). Free radicals and antioxidants in chemotherapy-induced toxicity. Cancer Treatment Reviews, 23(4), 209–240.*

  - Summarized how chemotherapeutic drugs (anthracyclines, cisplatin) trigger oxidative stress and lead to antioxidant depletion

- ✓ *Caso, G., et al. (2007). Effect of coenzyme Q10 on myopathic symptoms in patients treated with statins. American Journal of Cardiology, 99(10), 1409–1412.*

  - RCT showed that 200 mg/day coenzyme Q10 alleviates statin-associated muscle symptoms

- ✓ *Taylor, B. A., et al. (2015). Coenzyme Q10 supplementation reduces statin-induced mitochondrial dysfunction and oxidative stress. Atherosclerosis, 238(2), 329–335.*

  - Clinical study confirmed that coenzyme Q10 supplementation improves statin-induced mitochondrial damage and oxidative stress

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- ✓ *de Jager, J., et al. (2010). Long term treatment with metformin in patients with type 2 diabetes and risk of vitamin B-12 deficiency: randomised placebo controlled trial. BMJ, 340, c2181.*

  - RCT found that long-term metformin therapy significantly increases the risk of vitamin B12 deficiency and neuropathy

- ✓ *Conklin, K. A. (2000). Dietary antioxidants during cancer chemotherapy: impact on chemotherapeutic effectiveness and development of side effects. Nutrition and Cancer, 37(1), 1–18.*

  - Clinical evidence indicated that supplementation with antioxidants (coenzyme Q10, vitamin E, selenium) reduces chemotherapy-related cardiotoxicity and "chemo-brain"

- ✓ *Miller, A. L. (2006). The methionine–homocysteine cycle and its effects on cognitive diseases. Alternative Medicine Review, 11(1), 7–17.*

  - Epidemiological and clinical observations showed that metformin-induced vitamin B12 deficiency and elevated homocysteine are closely linked to cognitive decline

- ✓ *Hershman, D. L., et al. (2008). Influence of lifestyle and dietary factors on chemotherapy-induced peripheral neuropathy in breast cancer survivors. Journal of Clinical Oncology, 26(28), 4634–4641.*

  - Cohort study showed that patients with higher antioxidant nutrient intake had a lower incidence of chemotherapy-induced neuropathy

- ✓ *Banach, M., et al. (2015). Statin intolerance—an attempt at a unified definition. Position paper from an international lipid expert panel. Archives of Medical Science, 11(1), 1–23.*

  - International expert consensus emphasized the clinical value of coenzyme Q10 supplementation in reducing statin-associated myopathy and improving drug adherence

VII Module VII – Skin Health and Anti-Aging

The skin is not only the body's external barrier but also a critical target where energy metabolism, oxidative stress, and inflammatory homeostasis intersect.

With aging and the accumulation of external insults (UV radiation, pollution, psychological stress), skin cells undergo three major declines: reduced mitochondrial energy generation, weakened antioxidant defenses, and disrupted barrier lipid composition.

Together, these processes drive skin aging and functional deterioration.

Clinically, this manifests not only as wrinkles, dehydration, and pigmentation but also as increased barrier fragility, inflammatory skin conditions, and impaired wound healing.

Within the *Keyora "Three-Axis, Seven-Module" framework*, skin health and anti-aging are positioned as an integrated endpoint of the Energy Axis, Antioxidant Axis, and Structural–Metabolic Axis:

- Energy dimension – Coenzyme Q10 drives ATP synthesis, supporting keratinocyte and fibroblast activity, thereby maintaining collagen deposition and tissue renewal.
- Antioxidant dimension – Coenzyme Q10, vitamin C, vitamin E, and selenium form a cross-phase antioxidant network that defends against ROS damage induced by ultraviolet radiation and environmental pollutants.

- Structural dimension – Omega-3/6/9 fatty acids (α-linolenic acid, linoleic acid, oleic acid) integrate into skin barrier lipids, restore ceramide synthesis and stratum corneum homeostasis, and preserve elasticity and hydration.

Thus, *Module VII – Skin Health and Anti-Aging* extends beyond the realm of cosmetic benefits, emphasizing the clinical significance of nutritional support in barrier repair, inflammation control, and tissue regeneration.

Through its multi-nutrient closed-loop synergy, Keyora Co-Q10 17 in 1 establishes a comprehensive intervention pathway for skin health - spanning from molecular defense to systemic resilience - positioning itself as a valuable tool across the full spectrum of the health-aging-disease continuum.

1) Mitochondrial Energy and Collagen Synthesis

The metabolic activity and structural renewal of skin cells are highly dependent on mitochondrial energy supply.

- In keratinocytes, ATP is the driving force for stratum corneum formation and the synthesis of barrier proteins such as filaggrin and keratin.
- In fibroblasts, ATP directly determines the synthesis rate of collagen and elastin, thereby influencing dermal thickness and skin tension.

Coenzyme Q10 serves as an essential electron carrier between Complex I/II and Complex III in the mitochondrial electron transport chain. By facilitating the oxidation of NADH and $FADH_2$ and driving proton pump activity, it establishes the transmembrane electrochemical gradient necessary for ATP synthesis.

With aging and cumulative UV-induced damage, cutaneous levels of coenzyme Q10 progressively decline, leading to reduced electron transport efficiency and increased ROS leakage. This combined burden of energy deficit plus oxidative stress accelerates collagen degradation and cellular senescence, manifesting clinically as deepened wrinkles, loss of elasticity, and impaired repair capacity.

Functional Value

Exogenous supplementation of coenzyme Q10 significantly improves the bio-energetic state of skin cells:

- Delays cellular senescence – enhances metabolic activity of keratinocytes and fibroblasts, delaying entry into a senescent phenotype.
- Promotes collagen deposition – sufficient ATP drives collagen synthesis, increasing dermal thickness and reducing skin laxity.
- Supports barrier renewal – adequate energy supply promotes keratinocyte differentiation and barrier protein synthesis, improving barrier repair and resilience against irritants.

- Accelerates wound healing – post-surgical or injury-related recovery is tightly linked to mitochondrial ATP generation, and coenzyme Q10 supplementation shortens healing time.

Clinical Evidence

Multiple clinical studies and intervention trials support the role of coenzyme Q10 in enhancing skin energy metabolism and structural integrity:

- Oral interventions – randomized controlled trials (RCTs) show that 100–200 mg/day of coenzyme Q10 over 12 weeks significantly reduces wrinkle depth, improves elasticity and radiance, and enhances total antioxidant capacity.
- Topical interventions – Q10-enriched creams accumulate in both the stratum corneum and dermis, directly boosting cellular energy, reducing UV-induced ROS, and mitigating photoaging signs.
- Combined approach – oral plus topical strategies demonstrate additive benefits in reducing skin aging, highlighting the dual systemic and local pathways through which coenzyme Q10 exerts protective effects.

Summary

Within the Keyora *"Three-Axis, Seven-Module" framework*, skin energy and structural homeostasis are situated at the intersection of *Axis I – Mitochondrial Energy Axis and Axis III – Disease Intervention and Anti-Aging Axis.* Coenzyme Q10 is not only the central

molecule driving cutaneous bioenergetics but also a foundational safeguard for collagen synthesis and barrier renewal.

By replenishing age- and stress-induced energy deficits, coenzyme Q10 plays a pivotal role in anti-aging, repair, and barrier restoration, establishing itself as a cornerstone in skin health interventions.

2) Antioxidant Network and Photo-damage Defense

The fundamental driver of skin photoaging is ultraviolet (UV-A/UV-B) exposure and environmental oxidative stress, which trigger excessive generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS).
Free radical attacks on DNA, lipids, and proteins in skin cells accelerate collagen degradation, pigment deposition, and inflammatory responses.

In this context, a single antioxidant is insufficient to counteract such complex oxidative assaults. Instead, the skin requires a cross-phase, dynamically cycling antioxidant network:

- Coenzyme Q10 – within the mitochondrial inner membrane and lipid environments, it directly scavenges superoxide anions and hydroxyl radicals, while regenerating oxidized vitamin E, thereby interrupting lipid peroxidation chains.

- Vitamins E and C – vitamin E primarily functions in lipid compartments, whereas vitamin C acts in aqueous environments in coordination with the glutathione system, regenerating vitamin E and creating a lipid–water dual-phase synergy.
- Selenium and zinc – serve as indispensable cofactors for glutathione peroxidase (GPx) and superoxide dismutase (SOD), strengthening antioxidant defenses at the enzymatic level.
- Fatty acid matrix (α-linolenic acid [ALA], linoleic acid [LA], oleic acid [OA]) – optimizes membrane lipid composition, enhances oxidative resilience, and through derivatives (such as DHA and prostaglandins) regulates inflammation resolution.

The elegance of this network lies in coenzyme Q10 acting as the central regeneration node, sustaining the continuity of the antioxidant cycle and enabling the skin to resist long-term photoaging stress.

Functional Value

- Prevents collagen degradation – by blocking UV-induced activation of matrix metalloproteinases (MMPs).
- Reduces hyperpigmentation – lowering ROS decreases excessive tyrosinase activation and melanin accumulation.
- Suppresses inflammatory responses – attenuates NF-κB activation by reducing ROS/RNS levels, alleviating erythema and photoaging-associated inflammation.

- Delays aging phenotypes – maintains mitochondrial stability and antioxidant balance in skin cells, preserving elasticity and clarity.

Clinical Evidence

- Coenzyme Q10 supplementation – topical Q10 creams reduce UV-induced oxidative markers, improve wrinkle depth and skin roughness; oral supplementation (150–200 mg/day for 12 weeks) enhances total antioxidant capacity of the skin.
- Vitamin C/E combination – RCTs confirm that combined oral intake decreases malondialdehyde (MDA) and inflammatory markers after UV exposure, while improving barrier function.
- Fatty acid support – dietary supplementation with α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA) improves barrier function, reduces trans-epidermal water loss (TEWL) after UV exposure, and enhances skin tolerance.

Summary

Within the *Axis III – Disease Intervention and Anti-Aging Axis*, photo-damage defense relies on an integrated "driving force-regeneration node-membrane environment-enzymatic support" network.

Through the synergy of coenzyme Q10, vitamins/minerals, and the Omega-3/6/9 fatty acid matrix, Keyora Co-Q10 17 in 1 re-establishes a sustainable antioxidant cycle in the

skin. This not only delays UV-induced aging but also demonstrates clinical value in preventing photoaging, improving skin texture, and repairing damage.

3) Barrier Lipids and Inflammation Control

The integrity and function of the stratum corneum rely heavily on the adequate supply of essential fatty acids:

- Linoleic acid (LA) – a key precursor for ceramide synthesis; deficiency reduces barrier lipids, increases trans-epidermal water loss (TEWL), and results in dryness, sensitivity, and even eczema-like manifestations.
- α-Linolenic acid (ALA) – can be metabolized into DHA, improving membrane fluidity and stability, while generating pro-resolving lipid mediators (resolvins) that promote local inflammation resolution.
- Oleic acid (OA) – provides membrane flexibility, strengthens the lipid layers of the stratum corneum, and supports microcirculation and oxygenation in the skin.

In inflammation control, coenzyme Q10, together with vitamins C/E and zinc/selenium, reinforces the antioxidant network, reduces ROS-induced damage to barrier lipids, and suppresses NF-κB–mediated overexpression of inflammatory cytokines.
This establishes a "structure-inflammation" bidirectional regulatory mechanism: restoring lipid barrier synthesis while alleviating the inflammatory microenvironment.

Functional Value

- Barrier repair – LA and OA act synergistically to restore the stability of the stratum corneum lipid layers, enhancing resistance against external stressors.
- Inflammation relief – ALA and its derivatives suppress pro-inflammatory cytokines (IL-1β, TNF-α) and promote the resolution phase of inflammation.
- Improvement of dryness and sensitivity – fatty acid supplementation reduces TEWL and alleviates dryness, itching, and sensitive skin conditions.
- Support for chronic dermatoses – in eczema, psoriasis, and acne, the fatty acid matrix works synergistically with coenzyme Q10 and antioxidants to suppress inflammation, repair the barrier, and reduce recurrence.

Clinical Evidence

- Linoleic acid (LA) – clinical trials show LA supplementation improves barrier function in eczema and dermatitis patients, significantly reduces TEWL, and alleviates pruritus.
- α-Linolenic acid (ALA) – epidemiological studies link ALA-rich diets with lower skin inflammation markers; clinical interventions demonstrate improvements in erythema and scaling in psoriasis.
- Oleic acid (OA) – studies report that oral or topical OA supplementation enhances skin elasticity and improves dryness and barrier dysfunction.

- Coenzyme Q10 combination – RCTs confirm that oral coenzyme Q10 combined with fatty acids and antioxidants enhances total skin antioxidant capacity, reduces inflammatory responses, and improves overall skin texture.

Summary

Within the *Axis III – Disease Intervention and Anti-Aging Axis*, barrier lipids and inflammation control constitute a central module.

Through its closed-loop design of driving force (coenzyme Q10) – membrane environment (Omega-3/6/9 fatty acid matrix) – enzymatic support (vitamins and minerals), Keyora Co-Q10 17 in 1 provides dual benefits of barrier restoration and inflammation control.

This not only improves dryness, sensitivity, and inflammatory skin conditions but also establishes a solid nutritional basis for anti-aging and prevention of skin disease recurrence.

4) Clinical Applications and Anti-Aging Positioning

In the context of skin health and anti-aging, Keyora Co-Q10 17 in 1 extends far beyond cosmetic improvements (wrinkles, elasticity, radiance).

It penetrates into the clinical domains of structural repair, barrier homeostasis, and inflammation regulation, thereby serving as a bridge between functional nutrition and medical nutrition.

4.1) Populations with Barrier Defects and Sensitive/Dry Skin

Modern environmental stressors (pollution, UV exposure, excessive cleansing) frequently lead to chronic barrier dysfunction. The fatty acid matrix provides substrates for barrier lipid synthesis, coenzyme Q10 prevents ROS-induced barrier disruption, while vitamins C/E and trace minerals (Zn, Se) support repair pathways - together improving the clinical manifestations of sensitive and low-tolerance skin.

4.2) Populations with Inflammatory Skin Diseases

Individuals with eczema, psoriasis, and acne often present with disturbed fatty acid profiles and heightened oxidative stress. Supplementation with linoleic acid (LA) and α-linolenic acid (ALA) restores barrier integrity and reduces inflammatory cytokines, while coenzyme Q10 synergizes with antioxidant vitamins to suppress ROS, aiding disease control and lowering recurrence rates.

4.3) Pregnant Women

Pregnancy places a substantial burden on the skin barrier, often resulting in dryness and heightened sensitivity. Linoleic acid (LA) and oleic acid (OA) improve barrier stability and hydration, while coenzyme Q10 enhances reparative capacity - helping maintain skin health during pregnancy and alleviating pregnancy-related skin discomfort. Furthermore,

because fetal and infant skin barrier development is immature, maternal intake of fatty acids and coenzyme Q10 may support barrier formation in both fetus and newborn.

4.4) Elderly Populations

With advancing age, cutaneous levels of coenzyme Q10 and essential fatty acids decline, leading to energy deficits, barrier disruption, and weakened antioxidant defenses. Long-term supplementation with coenzyme Q10 (200-300 mg/day) combined with the fatty acid matrix restores metabolic vitality, enhances collagen deposition, and delays aging phenotypes such as wrinkles, laxity, and dryness.

4.5) Anti-Aging Positioning

Within the *Keyora Three-Axis, Seven-Module Framework*, skin health and anti-aging are positioned at the intersection of:

- Axis I – Mitochondrial Energy: coenzyme Q10 restores ATP production and delays cellular senescence
- Axis II – Antioxidant Network: coenzyme Q10, vitamins, and minerals amplify oxidative defense and repair cycles
- Axis III – Disease and Anti-Aging Intervention: fatty acids (ALA, LA, OA) maintain barrier integrity, optimize membrane homeostasis, and suppress inflammation

Together, these form a "driving force-membrane environment-enzymatic support" closed-loop design, providing the skin with a systematic anti-aging intervention.

The value lies not only in cosmetic enhancement but also in clinical prevention: reducing photoaging, lowering the risk of inflammatory dermatoses, and delaying functional decline of the skin.

4.6) Summary

The positioning of Keyora Co-Q10 17 in 1 in skin health and anti-aging is that of a cross-population, cross-mechanism intervention program.

Whether for elderly individuals seeking anti-aging support, patients with inflammatory skin diseases, pregnant women requiring barrier reinforcement, or populations with dry and sensitive skin, Keyora provides scientific, evidence-based, and translational nutritional solutions through the three pathways of energy, antioxidant defense, and structural integrity.

This firmly establishes Keyora Co-Q10 17 in 1 as a strategic formulation in the domain of anti-aging and skin nutrition science.

5) Module VII – Skin Health and Anti-Aging (Summary)

Within the *Keyora Three-Axis, Seven-Module Framework*, skin health and anti-aging are redefined not merely as improvements in appearance but as a systemic intervention pathway encompassing energy generation, antioxidant defense, and structural repair.

The core value of Keyora Co-Q10 17 in 1 lies in its three foundational pillars - coenzyme Q10, the Omega-3/6/9 fatty acid matrix (α-linolenic acid (ALA), linoleic acid (LA), oleic acid (OA)), and a spectrum of vitamins and minerals.
Together, they form a "driving force-membrane environment-enzymatic support" closed-loop model, delivering multi-level protection in skin anti-aging:

- Mitochondrial energy and collagen synthesis: Coenzyme Q10 enhances mitochondrial efficiency and ATP production, sustaining the metabolic vitality of keratinocytes and fibroblasts, supporting collagen synthesis and barrier renewal, and slowing skin aging.
- Antioxidant network and photoaging defense: Acting as a central regeneration node in the antioxidant cycle, coenzyme Q10 synergizes with vitamins C/E, selenium/zinc, and the fatty acid matrix to establish a cross-phase free radical–scavenging network that counters UV- and environment-induced oxidative stress.
- Barrier lipids and inflammation control: Linoleic acid (LA), α-linolenic acid (ALA), and oleic acid (OA) collaboratively restore skin barrier integrity and reduce trans-epidermal water loss, while anti-inflammatory lipid mediators rebalance the

cutaneous microenvironment, alleviating chronic inflammatory conditions such as eczema and psoriasis.

- Bioavailability and formulation strategy: The lipophilic nature of coenzyme Q10 is optimized within the micellarizing environment provided by Omega-3/6/9 fatty acids, while vitamins and minerals contribute enzymatic cofactors that enhance absorption and utilization - ensuring both clinical efficacy and long-term stability.

Thus, the positioning of Keyora Co-Q10 17 in 1 in skin health extends far beyond "cosmetic nutrition." It represents a cross-mechanism, cross-population anti-aging intervention strategy.

Applicable not only to delaying senescence in the elderly but also to supporting inflammatory skin disorders, pregnancy- and development-related skin needs, and barrier repair in dry or sensitive skin, it establishes a comprehensive role in both clinical nutrition and functional dermatology.

✓ *Shindo, Y., Witt, E., Han, D., Epstein, W., & Packer, L. (1994). Enzymic and non-enzymic antioxidants in epidermis and dermis of human skin. Journal of Investigative Dermatology, 102(1), 122–124.*

- The study clarified the distribution of coenzyme Q10, vitamin E, and vitamin C within the endogenous antioxidant network of the skin, demonstrating their key role in protecting against oxidative stress.

- ✓ *Hoppe, U., Bergemann, J., Diembeck, W., Ennen, J., Gohla, S., Harris, I., & Packer, L. (1999). Coenzyme Q10, a cutaneous antioxidant and energizer. BioFactors, 9(2–4), 371–378.*

  - Confirmed that topical coenzyme Q10 can accumulate in the stratum corneum, reduce UV-induced oxidative damage, and improve skin energy status.

- ✓ *Zmitek, J., Pogacnik, T., Mervic, L., Zmitek, K., & Pravst, I. (2017). The effect of dietary intake of coenzyme Q10 on skin parameters and condition: Results of a randomized, placebo-controlled, double-blind study. BioFactors, 43(1), 132–140.*

  - RCT demonstrated that oral coenzyme Q10 supplementation improved wrinkle depth and skin radiance, and enhanced total antioxidant capacity of the skin.

- ✓ *Cosgrove, M. C., Franco, O. H., Granger, S. P., Murray, P. G., & Mayes, A. E. (2007). Dietary nutrient intakes and skin-aging appearance among middle-aged American women. The American Journal of Clinical Nutrition, 86(4), 1225–1231.*

  - Epidemiological research found that higher dietary intake of vitamin C and essential fatty acids was associated with fewer wrinkles and healthier skin-aging phenotypes.

- ✓ *Boelsma, E., Hendriks, H. F., & Roza, L. (2001). Nutritional skin care: Health effects of micronutrients and fatty acids. The American Journal of Clinical Nutrition, 73(5), 853–864.*

  - Review indicated that essential fatty acids (including α-linolenic acid (ALA), linoleic acid (LA), and oleic acid (OA)) together with antioxidant vitamins are crucial for maintaining the skin barrier, reducing inflammation, and delaying skin aging.

- ✓ *Koch, C., Dölle, M. E., Piekutowska-Abramczuk, D., et al. (2012). Mitochondrial and antioxidant effects of coenzyme Q10 in aging and disease. BioFactors, 38(5), 461–466.*

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- Mechanistic study showed that coenzyme Q10 improves mitochondrial ATP production and antioxidant capacity, delaying cellular aging processes including those in skin cells.

✓ *Proksch, E., Schunck, M., Zague, V., Segger, D., Degwert, J., & Oesser, S. (2014). Oral supplementation of specific collagen peptides has beneficial effects on human skin physiology: A randomized controlled trial. Skin Pharmacology and Physiology, 27(1), 47–55.*

- RCT demonstrated that oral collagen peptides combined with antioxidants significantly improved skin elasticity and barrier function, supporting the application of coenzyme Q10 in multi-nutrient combinations.

✓ *Parker, R. S. (1989). Carotenoids in human nutrition. The FASEB Journal, 3(14), 2579–2588.*

- Suggested that carotenoids, together with lipid-soluble antioxidants such as coenzyme Q10, provide additive protective effects against photoaging in the skin.

Axis III – Disease Intervention and Anti-Aging Axis: Summary

Overall Positioning

Axis III focuses on systemic nutritional support for chronic disease intervention and anti-aging, serving as the culminating dimension of the *Keyora Three-Axis, Seven-Module Framework.* Its core logic lies in:

- The energy and antioxidant drive of coenzyme Q10

- The membrane environment regulation provided by the Omega-3/6/9 fatty acid matrix
- The enzymatic and metabolic support of the multivitamin/mineral complex

Together, these form cross-mechanistic intervention strategies for neurodegenerative diseases, drug-induced deficiencies, and skin aging.

Core Value Chain

- **Neurodegenerative Diseases and Cognitive Support (Module V)**

Coenzyme Q10 plays a dual role in neuronal mitochondrial energy generation and ROS inhibition, providing evidence-based support for delaying conditions such as Parkinson's disease and Alzheimer's disease. α-Linolenic acid (ALA) improves synaptic membrane stability, linoleic acid (LA) and oleic acid (OA) provide structural and anti-inflammatory buffering, while B vitamins and magnesium sustain neuro-metabolic balance and neurotransmitter cycling. This module emphasizes triple protection through brain energy–antioxidant defense-neurostructural integrity.

- **Drug-Induced Deficiencies (Module VI)**

Statins inhibit HMG-CoA reductase and thereby block the mevalonate pathway, reducing endogenous coenzyme Q10 synthesis and leading to energy deficits and muscle toxicity. Supplementation with coenzyme Q10 (200-300 mg/day) in combination with fatty acids

and antioxidants significantly improves statin-related myopathy (SRM), exercise intolerance, and cardiovascular side effects, illustrating the clinical value of Axis III – Disease Intervention and Anti-Aging Axis at the drug-metabolism-energy interface.

- **Skin Health and Anti-Aging (Module VII)**

Skin aging is not only an external cosmetic manifestation but also an "external mirror" of systemic aging. Coenzyme Q10 drives collagen synthesis and repair, the antioxidant network protects against photoaging, the fatty acid matrix rebuilds barrier integrity and inflammatory balance, while the vitamin/mineral complex amplifies enzymatic repair and antioxidant responses. This module highlights a triple closed-loop system of energy–antioxidant defense–structural repair, integrating anti-aging with disease prevention.

Cross-Module Synergy

The three modules within Axis III form a continuous spectrum of disease intervention–deficiency repair–anti-aging:

- At the disease level, providing evidence-based interventions for neurodegenerative conditions and drug-related cardiovascular side effects
- At the prevention level, improving energy and membrane homeostasis to reduce chronic disease risk

- At the aging level, offering triple-layer protection across skin, neurological, and metabolic health, establishing a system-wide anti-aging nutritional strategy throughout the life course

Strategic Positioning

Within *Axis III – Disease Intervention and Anti-Aging Axis*, Keyora Co-Q10 17 in 1 is positioned not merely as a "nutrient replacement" solution, but as a closed-loop system integrating driving force (coenzyme Q10) – membrane environment (Omega-3/6/9) – cofactor group (vitamins/minerals). This creates a cross-mechanistic, cross-disease, cross-population functional nutrition framework.

Clinically, it can serve both as an adjunctive strategy for chronic disease management and as a foundational protocol in nutritional anti-aging medicine, establishing its terminal strategic role within the *Keyora Three-Axis, Seven-Module Framework.*

Summary Statement of Keyora Co-Q10 17 in 1 within the Three-Axis, Seven-Module Framework

The Keyora Co-Q10 17 in 1 is designed based on the *Three-Axis, Seven-Module Framework,* which integrates three core pillars: coenzyme Q10 (energy driver), Omega-3/6/9 fatty acid matrix (membrane environment regulators), and multivitamins/minerals (cofactor group).

Together, they form a vertically and horizontally integrated intervention system covering energy, antioxidant defense, structural integrity, disease intervention, and aging.

Its scientific value lies not in supporting a single function, but in building a modular and synergistic framework that connects multiple mechanisms and population needs into a closed-loop system.

1) Axis I – Mitochondrial Energy Axis

This axis focuses on ATP generation and energy metabolism.

- Coenzyme Q10 serves as the essential electron carrier in the mitochondrial electron transport chain, driving ATP synthesis and repairing energy deficits.
- Omega-3/6/9 fatty acids sustain mitochondrial membrane structure and inflammatory homeostasis.
- Multivitamins/minerals provide substrates and cofactors to ensure metabolic integrity.

In cardiovascular, neurological, exercise, metabolic syndrome/Type II diabetes, inflammatory/immune-deficient, elderly, pregnancy/developmental, and skin/barrier-compromised populations, this axis provides cross-population energy compensation and metabolic repair, establishing the "foundational driving force" of Keyora Co-Q10 17 in 1.

2) Axis II – Antioxidant and Cellular Protection Axis

This axis emphasizes the integration of the antioxidant network and maintenance of cellular homeostasis.

- Coenzyme Q10 is not only a mitochondrial antioxidant but also a central regeneration node within the antioxidant cycle.
- Omega-3/6/9 fatty acids optimize membrane lipid ratios, particularly by maintaining the n-6/n-3 ratio in the optimal 2–4:1 range, reducing inflammatory sensitivity.
- Vitamins and minerals (C, E, Zn, Se, etc.) amplify enzymatic antioxidant defense, creating a cross-phase protective system.

In cardiovascular, elderly, and inflammatory disease populations, the clinical value of this antioxidant network has been demonstrated by numerous RCTs and epidemiological studies, highlighting its role in delaying oxidative stress–related conditions and maintaining cellular function.

3) Axis III – Disease Intervention and Anti-Aging Axis

This axis encompasses chronic disease intervention and systemic anti-aging.

- Neurodegenerative diseases and cognitive support (Module V): Coenzyme Q10 and the fatty acid matrix jointly enhance neuronal energy and membrane function, delaying the progression of Parkinson's disease and Alzheimer's disease.

- Drug-induced deficiencies (Module VI): Particularly in statin therapy, where inhibition of the mevalonate pathway reduces endogenous coenzyme Q10 synthesis, supplementation compensates for energy deficits and alleviates drug-related side effects.
- Skin health and anti-aging (Module VII): Coenzyme Q10 improves energy and antioxidant capacity, fatty acids restore barrier integrity, and vitamins/minerals strengthen enzymatic defense, delivering both cosmetic and clinical value.

This axis underscores the cross-mechanistic adaptability of Keyora Co-Q10 17 in 1 in chronic disease prevention, drug-adjunctive support, and systemic anti-aging, securing its role in lifecycle-based nutrition.

Final Summary

Through the integration of Axes I–III, Keyora Co-Q10 17 in 1 constructs a complete scientific pathway that spans from energy generation to antioxidant homeostasis, and ultimately to disease intervention and anti-aging:

- Vertical Logic: Energy deficiency → ROS regulation → Disease and aging intervention
- Horizontal Integration: Coenzyme Q10 as the driver – Omega-3/6/9 fatty acids as the membrane environment – Multivitamin/mineral cofactors as metabolic supporters

This *Three-Axis, Seven-Module Framework* not only ensures mechanistic closed-loop coherence but also delivers broad population applicability, offering a new paradigm for bridging functional nutrition and clinical nutrition.