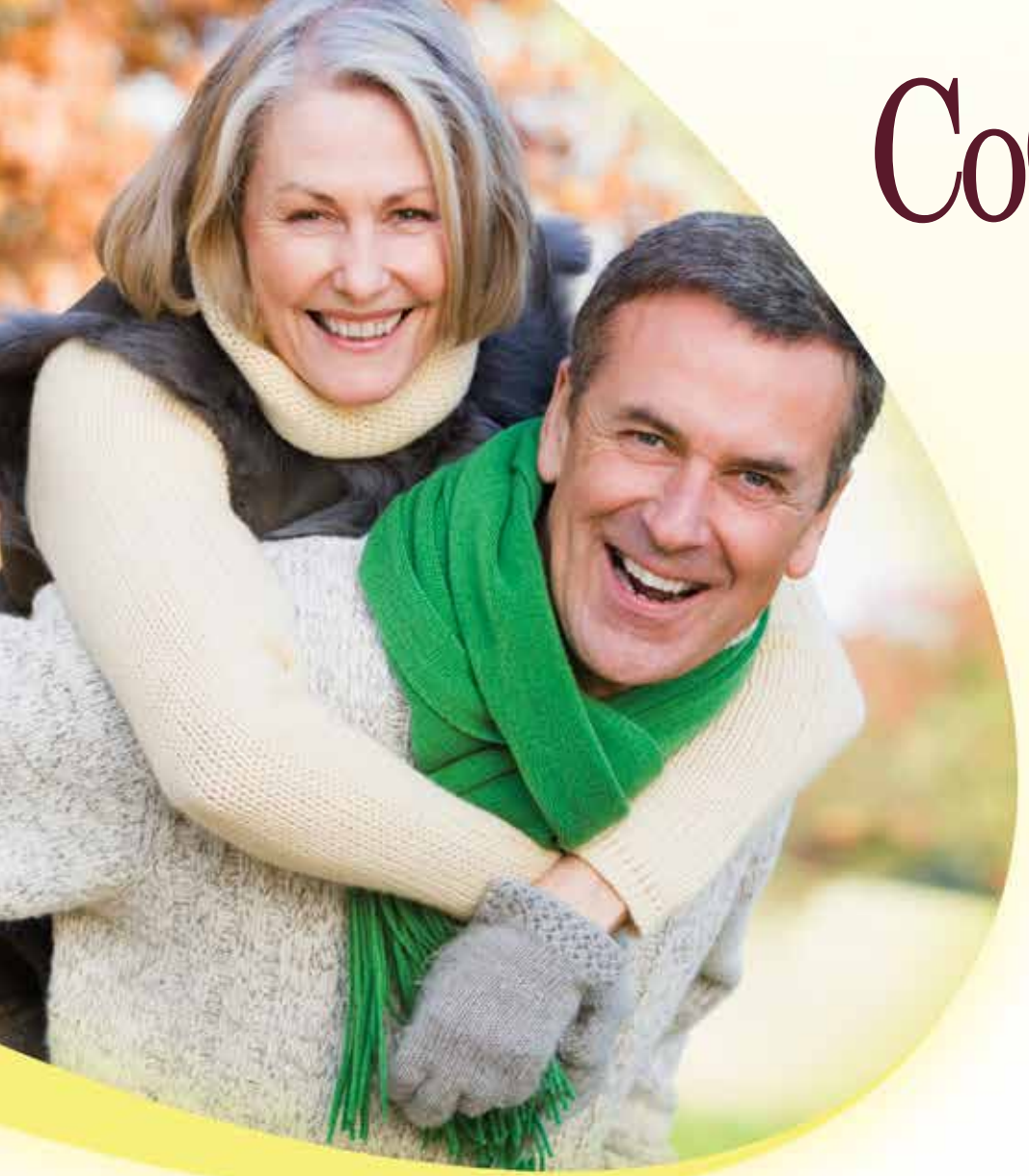
CoQsol-CF®



A completely soluble,

100% crystal-free

formulation clinically

proven to provide superior

bioavailability of CoQ_{10}

SOFT GEL
TECHNOLOGIES, INC.

The Crucial Nature of CoQ_{10}

Coenzyme Q_{10} (CoQ_{10}) is a vitamin-like substance found in virtually all cells of the human body, including the heart, liver, and skeletal muscles, and in most plant and animal cells.

- As an **antioxidant**, CoQ_{10} protects proteins, LDL ("bad") cholesterol, and mitochondrial DNA from oxidative damage.
- As a participant in the production of **cellular energy**, CoQ_{10} helps ensure the body's biggest energy consumers — the heart and the brain — are well-fed.

Thanks to these two crucial functions, CoQ_{10} can lower blood pressure, enhance cardiac function in patients with cardiomyopathy, improve symptoms of congestive heart failure, relieve angina, and increase recovery from heart attack. Additionally, it may slow the progression and improve the symptoms of neurodegenerative diseases such as Parkinson's disease. Of course, none of these benefits can be realized if CoQ_{10} isn't absorbed — and research indicates that the body uptakes only a small fraction of traditional powder-based (crystalline) CoQ_{10}.

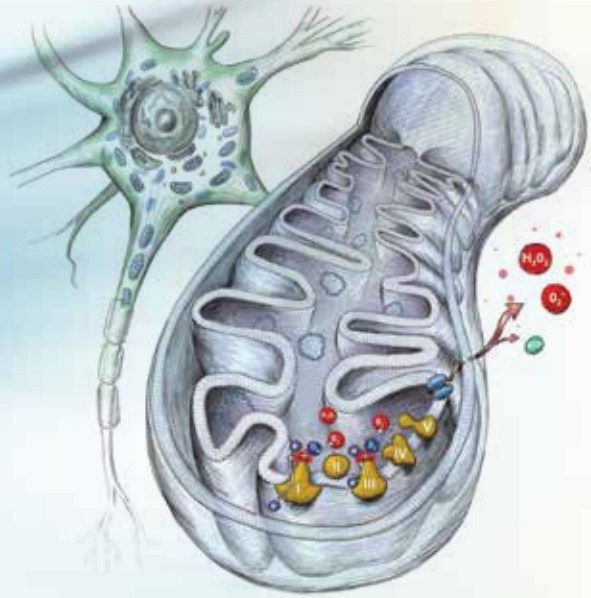


Illustration by N.R. Fuller, Sayo-Art.

The CoQ_{10} Absorption Dilemma

In order to be absorbed, all nutrients must first be in a water-soluble form. Unfortunately, because of its structure, CoQ_{10} is highly lipophilic (fat-loving) — and practically insoluble in water. This lipophilic nature makes CoQ_{10}'s absorption:

- **Poor:** Less than 6% of orally administered CoQ_{10} permeates the gastro-intestinal tract into the blood.
- **Highly variable:** Some individuals absorb considerably less CoQ_{10} than others.
- **Strongly dependent on stomach contents:** Foods rich in fat enhance absorption.

Making matters worse, CoQ_{10} is a **large molecule**, contributing to its poor absorption. Plus, when CoQ_{10} is produced commercially, crystals are formed that melt when they reach 118°F or 48°C. Upon cooling, CoQ_{10} recrystallizes, which frequently results in even **larger crystals** — and further lowers CoQ_{10} bioavailability.

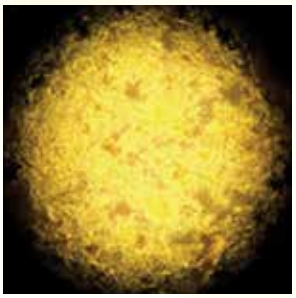
The Crystal-Free CoQ_{10} Solution:

CoQsol-CF®

In order to improve bioavailability, some manufacturers have sought to reduce the particle size of CoQ_{10}, thus increasing its surface area. Suspending fine particles in an emulsion or paste is an effective means of increasing bioavailability. However, there is an even more effective solution: achieving complete solubility.

*Introducing **CoQsol-CF® from Soft Gel Technologies**, a completely soluble, liquid, crystal-free solution of CoQ_{10} clinically proven to provide superior bioavailability of this key nutrient.*

Solubility → **Bioavailability** → **Absorption**



CoQ_{10} Paste

CoQsol-CF® is a unique, patent-pending formulation of CoQ_{10}, d-Limonene, and natural tocopherols (vitamin E). Upon microscopic examination at 200x, a paste of CoQ_{10} powder and soybean oil exhibits a crystalline structure, while CoQsol-CF® is completely devoid of crystals because the CoQ_{10} has been solubilized.

CoQsol-CF®

CoQsol-CF®: Trio of Ingredients

- **CoQ_{10}:** CoQ_{10} functions as a carrier to transfer electrons across the membrane of the mitochondria — the energy-producing "factories" within cells — to drive production of adenosine triphosphate (ATP), or cellular energy. Heart muscles have the greatest concentration of mitochondria — 5,000 per cell — which is one reason why CoQ_{10} is so important for cardiovascular function.

  In its reduced form, ubiquinol, CoQ_{10} acts as an antioxidant to protect proteins, LDL ("bad") cholesterol, and mitochondrial DNA from oxidative damage. Research has shown that CoQ_{10} supplementation exerts a sparing effect on vitamin E in healthy subjects, helping to maintain its antioxidant state. It also reduces levels of lipid peroxidation — the pivotal reaction in the cause of atherosclerosis — and thus reduces the risk of cardiovascular disease.

- **d-Limonene:** Extracted from the oil of citrus fruits, food-grade d-Limonene acts as a non-polar organic solvent that solubilizes CoQ_{10}, without causing significant chemical interactions or degradation.[1] The end result is a liquid, crystal-free, completely soluble CoQ_{10} — providing superior bioavailability — that does not require heat or synthetic, chemical solvents and that fully resists recrystallization at ambient temperatures.

- **Tocopherols:** A form of vitamin E, tocopherols enhance the biological function of CoQ_{10}, which in turn helps maintain the antioxidant state of vitamin E.

Several factors can deplete CoQ_{10} levels in the body:

- Aging
- Certain medications, such as statin drugs
- Certain disease states

It has also been established that people with a variety of cardiovascular disorders — including congestive heart failure, hypertension, aortic and mitral valve diseases, diabetic cardiomyopathy, and congenital valvular defects — are prone to myocardial CoQ_{10} deficiency.

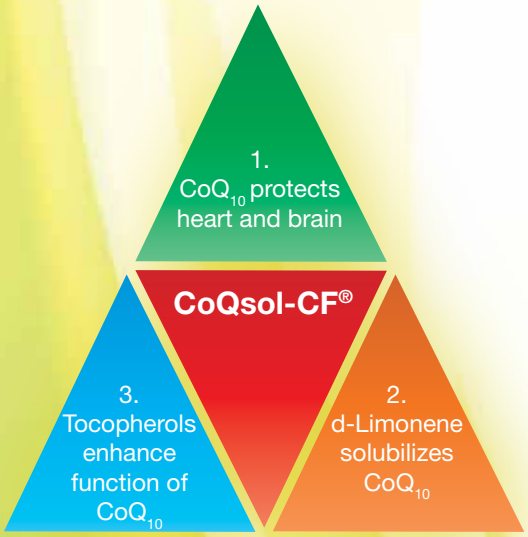
CoQsol-CF®

Proof of Bioavailability

Particle Size Analysis

Investigators at the third-party laboratory Particle Technology Labs, Inc. performed particle size analysis on CoQsol-CF® using a variety of methods:

- **High-intensity microscope light**. A sample of CoQsol-CF® was placed into a clear glass vial. When a high-intensity microscope light was directed through the container, no scattered light was observed, due to near sub-micron particulate matter.
- **100x dark field microscope**. A sample of CoQsol-CF® was placed under a 100x dark field microscope, which is able to detect the presence of very small particles. There was no evidence of large crystalline — nor of near-micron sized — particulate matter.
- **Instrumental analysis**. A sample of CoQsol-CF® was placed into several instruments able to detect particulate material down to at least 1 part per million. No submicron particulate was detected.



in vivo Research

"Bioavailability and Tissue Distribution of Soluble vs. Powdered Coenzyme Q_{10}"

An *in vivo* study was undertaken to compare the bioavailability and tissue distribution of various forms of CoQ_{10}.

Forty eight male mice were randomly assigned to four treatment groups: 1. CoQsol-CF®, 2. CoQsol Standard, 3. Powdered CoQ10, or 4. Placebo. Each group received the treatment by gavage for 4 weeks. The study yielded the following results:

- Overall **concentration of CoQ_{10}** was highest in the CoQsol-CF® group.
- Treatment with CoQsol-CF® resulted in accumulation of CoQ_{10} in the serum, heart, and liver — the normal CoQ_{10} storage organs — suggesting the **best bioavailability**.
- **~ 20% more CoQ_{10} was available** in the hearts of mice treated with CoQsol-CF® compared to other treatment groups.
- **~ 18% more CoQ_{10} was available** in the livers of mice treated with CoQsol-CF® compared to other treatment groups.

"We were taken by the fact that the fluid was sparkling clean to the naked eye under a high-intensity light beam."

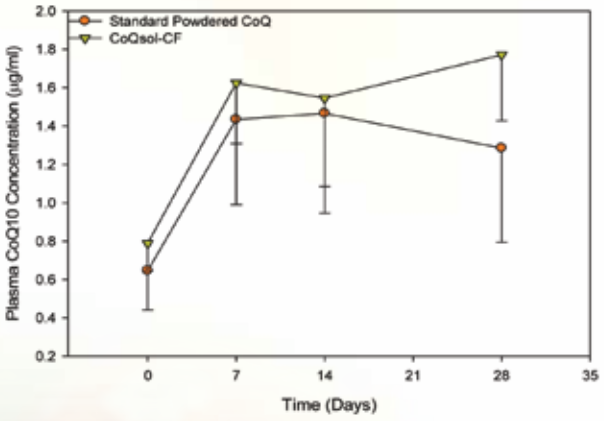
- Investigators at the 3rd party laboratory Particle Technology Labs, Inc.

Human Clinical Research

"Bioavailability and Health Effects of CoQ_{10} in Healthy Human Adults"

A double-blind, randomized, parallel group human clinical trial was undertaken to compare the oral bioavailability of CoQsol-CF® versus standard, commercial-grade Powdered CoQ_{10} in 30 healthy subjects over a period of 28 days. Compared to supplementation with standard Powdered CoQ_{10}, supplementation with CoQsol-CF® resulted in:

- Significantly **greater uptake** of CoQ_{10}.
- Significantly **increased plasma CoQ_{10} levels** by the end of the treatment period.
- Significantly **higher post-treatment** oral bioavailability of CoQ_{10}.
- Significantly **higher retention of plasma CoQ_{10} levels** above baseline up to 6 days post-treatment.



"Peak Absorption Characteristics and Steady State Bioavailability of a Cold Soluble CoQ_{10} Product"

A pilot clinical trial was undertaken to determine the single-dose peak absorption characteristics and the 28-day steady state bioavailability of CoQsol-CF® in 5 normal volunteers.

Peak Absorption Study Volunteers took 60 mg CoQsol-CF®, followed by a breakfast of orange juice or milk with a bagel or cereal.

- 4 hours after ingesting the supplement, group plasma CoQ_{10} levels increased significantly from 0.88 µg/ml (baseline) to 1.36 µg/ml.
- Peak plasma levels occurred at 6 hours (Tmax) and the maximum plasma concentration (Cmax) was 2.28 µg/ml.
- The amount of CoQ_{10} absorbed at Cmax was 4,769.5 µg/ml, or 7.96% of the ingested dose — significantly higher than most forms of CoQ_{10}.

Steady State Plasma CoQ_{10} Bioavailability Volunteers continued taking 60 mg CoQsol-CF® daily with breakfast for 28 days.

- At 7 days, the mean plasma CoQ_{10} level had increased to 2.39 µg/ml.
- At 14 days, the mean plasma CoQ_{10} level had increased to 2.68 µg/ml.
- At 28 days, the mean plasma CoQ_{10} level had reached 2.75 µg/ml. *This means that in just 4 weeks, the mean CoQ_{10} plasma level increased by 200%.*

"Overall, the results of this study suggest that CoQ_{10} in the CoQsol-CF® formulation is taken up better and provides a longer oral bioavailability compared to the standard, Powdered CoQ_{10} formulation."

- Crowley D.C., et al. "Bioavailability and Health Effects of CoQ10 in Healthy Human Adults." May 11, 2006.

Indications

Cardiovascular Wellness

Thanks to its function as an antioxidant and its role in the production of cellular energy, supplemental CoQ_{10} has been shown to benefit patients with cardiovascular diseases, including:

- **Hypertension** (high blood pressure): A pilot study showed that in patients with hypertension, CoQ_{10} supplementation led to statistically significant decreases in systolic and diastolic blood pressure.[2]
- **Congestive heart failure** (a disease in which the heart does not adequately maintain circulation): At least five double-blind, placebo-controlled trials have found that CoQ_{10} significantly reduces the severity of symptoms in congestive heart failure patients.[3]
- **Cardiomyopathy** (heart muscle disease): Two studies have yielded very positive results in treating cardiomyopathy with CoQ_{10}. In each study, over 80% of patients showed significant improvements in cardiac function.[4]
- **Angina pectoris** (chest pain): Several small trials have shown that CoQ_{10} supplementation decreases angina episodes and increases exercise capacity.[5,6]
- **Heart attack recovery:** A double-blind trial found that heart attack survivors who supplemented with CoQ_{10} for 28 days afterwards experienced fewer heart-related problems than those who took placebo.[7]

CoQ_{10} supplementation has also been demonstrated to prevent the plasma CoQ_{10} decrease caused by the statin drug simvastatin — without affecting its cholesterol-lowering effect.[8]

Brain Wellness

There is substantial evidence that oxidative damage and mitochondrial dysfunction may play a key role in the pathogenesis of neurodegenerative diseases, including:

- **Parkinson's disease**. Two trials have indicated that CoQ_{10} supplementation may slow the progression of Parkinson's[9] and produce a mild improvement in symptoms.[10]
- **Alzheimer's disease**. While no clinical trials have been published on CoQ_{10} and Alzheimer's disease, researchers at a 2004 meeting of AcademyHealth did note that: "Because mitochondrial dysfunction has been postulated in AD, a randomized controlled trial of CoQ appears warranted."[11]

CoQsol-CF® Delivery Systems

CoQsol-CF® is an off-the-shelf formulation available in two shell varieties, each with the same fill ingredients: our original opaque mustard-colored gelatin shells and our new translucent amber-colored gelatin shells.

As a completely soluble, liquid, crystal-free solution of CoQ_{10} clinically proven to provide superior bioavailability, CoQsol-CF® is the CoQ_{10} of choice for discriminating manufacturers.

References

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2. **Yamagami T, et al**. Bioenergetics in clinical medicine. Studies on coenzyme Q_{10} and essential hypertension. *Res Commun Chem Pathol Pharmacol*. 1975; 11:273.

3. **EBSCO Publishing**. "Congestive Heart Failure." *Consumerlab.com*. Accessed June 9, 2009. http://www.consumerlab.com/tnp.asp?chunkiid=21583#ref2

4. **EBSCO Publishing**. "Cardiomyopathy." *Consumerlab.com*. Accessed June 9, 2009. http://www.consumerlab.com/tnp.asp?chunkiid=21484#ref1

5. **Kamikawa T, et al**. Effects of coenzyme Q_{10} on exercise tolerance in chronic stable angina pectoris. *Am J Cardiol*. 1985 Aug 1;56(4):247-51.

6. **Wilson, MR, et al**. Coenzyme Q_{10} therapy and exercise duration in stable angina. In: Folkers, K., Littami, GP, Yamogami, T (eds), *Biomedical and Clinical Aspects of Coenzyme Q10*, vol. 6, Amsterdam. Elsevier;1991:339-348.

7. **Singh RB, et al**. Randomized double-blind placebo-controlled trial of coenzyme Q_{10} in patients with acute myocardial infarction. *Cardiovasc Drugs Ther*. 1998;12:347-353.

8. **Bargossi AM et al**. Exogenous CoQ_{10} supplementation prevents plasma ubiquinone reduction induced by HMG-CoA reductase inhibitors. *Mol Aspects Med*. 1994; 15:S187.

9. **Shults CW, et al**. Effects of coenzyme Q10 in early Parkinson disease: evidence of slowing of the functional decline. *Arch Neurol*. 2002;59:1541-1550.

10 **Muller T, et al**. Coenzyme Q(10) supplementation provides mild symptomatic benefit in patients with Parkinson's disease. *Neurosci Lett*. 2003;341:201-204.

11 **Young AJ, et al**. Coenzyme Q_{10}: A Promising Treatment for Alzheimer's Disease? *Abstr AcademyHealth Meet*. 2004; 21: abstract no. 1715.

Highlights

Available exclusively from Soft Gel Technologies, CoQsol-CF® is a completely soluble, 100% crystal-free formulation clinically proven to provide superior bioavailability of CoQ_{10}.

CoQsol-CF® includes the following trio of ingredients:

- **CoQ_{10}**. CoQ_{10} serves two main functions in the body. As an antioxidant, CoQ_{10} protects proteins, LDL ("bad") cholesterol, and mitochondrial DNA from oxidative damage. As a participant in the production of cellular energy, CoQ_{10} helps ensure the body's biggest energy consumers — the heart and the brain — are well-fed.

- **d-Limonene**. Extracted from the oil of citrus fruits, food-grade d-Limonene acts as a non-polar organic solvent that solubilizes CoQ_{10}, without causing significant chemical interactions or degradation.

- **Tocopherols**. A form of vitamin E, tocopherols enhance the biological function of CoQ_{10}, which in turn helps maintain the antioxidant state of vitamin E.

CoQ_{10}

d-Limonene

Tocopherols

Why CoQsol-CF®?

- **Several factors can deplete CoQ_{10}.** Research shows that aging, certain medications such as statin drugs, and certain disease states can deplete CoQ_{10} levels in the body. Therefore, for many people, supplementation is indicated to replenish CoQ_{10} stores to normal levels.
- **CoQ_{10} in powder (crystalline) form is difficult to absorb.** Because of its highly lipophilic (fat-loving) structure, CoQ_{10} is practically insoluble in water, making its absorption poor, highly variable, and strongly dependent on stomach contents. Plus, the CoQ_{10} molecule is large in size, contributing to its poor absorption, and when heated and re-cooled, even larger crystals are created.
- **The most effective solution for achieving CoQ_{10} bioavailability is complete solubility.** Suspending fine particles of CoQ_{10} in an emulsion or paste is an effective means of increasing bioavailability. However, the most effective solution is to achieve *complete solubility*. CoQsol-CF® is a completely soluble, liquid, crystal-free solution of CoQ_{10}.
- **CoQsol-CF® is proven bioavailable.** Particle size analysis, *in vivo* research, and human clinical studies have all demonstrated the enhanced bioavailability of CoQsol-CF®. A double-blind, randomized, parallel human clinical trial found that supplementation with CoQsol-CF® resulted in: significantly increased plasma CoQ_{10} levels, significantly greater uptake of CoQ_{10}, significantly higher post-treatment oral bioavailability, and significantly higher retention of plasma CoQ_{10} levels above baseline up to 6 days post-treatment.

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