# MicroActive® CoQ10 Overview

Superior bioavailability and guaranteed uniform absorption

## MicroActive® CoQ10

MicroActive® CoQ10 complex in crystalline form supports uniform absorption and time release claims. In addition, if taken at higher doses, claims for heart and circulatory health benefits can be made, and can provide assurance of doubling CoQ10 levels in three weeks.

**MicroActive® CoQ10 Complex is a 26% CoQ10 free-flowing powder, clinically proven to offer:**

- Superior bioavailability
- 24-hour time release
- Uniformly enhanced absorption in all users

## Win in the Milligram Wars

CoQ10 is one of the most studied and beneficial active ingredients in health maintenance. Consumers recognize its benefits. Mass- market consumers often compare products based on the total amount of CoQ10 per dose, while not taking into account the issue of bioavailability.

CoQ10 is poorly absorbed for two primary reasons: CoQ10 molecules occur naturally in crystals, bound to each other in a form that is too large for cells to absorb. CoQ10 is also fat-soluble, and is relatively difficult to transport through the digestive system as compared to molecules that are water-soluble.

Some products attempt to overcome poor absorption and attract customers with high CoQ10 doses. The higher the dose, however, the lower the percentage absorbed. Spacing out consumption has some benefit, but it is inconvenient and may lead to inconsistent dosing. Finally, a number of individual factors such as diet, age, cholesterol levels, and gender create large differences from person to person in the quantities of and time required for CoQ10 absorption.

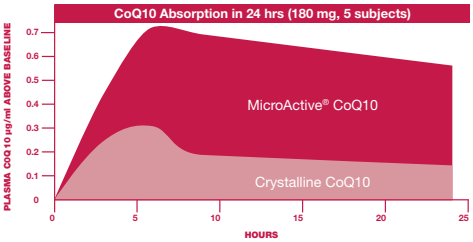
Other products use various technologies to address these issues. They depend on a combination of breaking up or melting the CoQ10 crystals, using surfactants in an oil medium to keep the molecule dissolved, and adding secondary ingredients to promote absorption (surfactants taken over time, however, have been shown to cause stomach irritation). Studies indicate that these solubilized products may provide uptake benefits for some people but not others. Furthermore, solubilized products in softgel form are expensive, inflexible, and have side effects for some users.

The patented MicroActive® process (U.S. 7,030,102) complexes each CoQ10 molecule with two ß-cyclodextrin molecules in a water media. ß-cyclodextrin is used extensively in the food and pharmaceutical industries. It is a GRAS compound formed through an enzymatic conversion of starch. One side of the molecule is fat-soluble and holds the CoQ10, while the other side is water-soluble and makes for efficient transport through the digestive system.

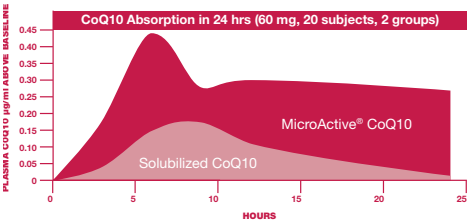
When the micronized MicroActive® complex arrives at a cell, it comes apart, depositing a single CoQ10 molecule for efficient absorption.

Six clinical studies compared MicroActive® CoQ10 to crystalline and solubilized products. The results demonstrate the clear advantages of MicroActive®.

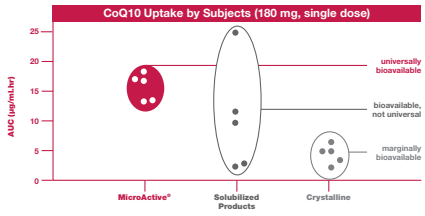
## Absorption Performance
## MicroActive® vs Crystalline CoQ10




## Absorption Performance
## MicroActive® vs Oil Solubilized CoQ10 Softgel




## Individual Subject's CoQ10 Absorption After Single Oral Dose




## Absorption Results

| Comparisons | Conditions | |
|---|---|---|
| MicroActive® vs Crystalline | 24 hr 180 mg 5 Ss | 370% better ($p<0.0001$) |
| MicroActive® vs Solubilized | 24 hr 180 mg 5 Ss | 158% better ($p<0.05$) |
| MicroActive® vs Solubilized | 24 hr 60 mg 20 Ss | 268% better ($p<0.006$) |
| MicroActive® vs Solubilized | 3 weeks 60 mg 20 Ss | 70% better ($p<0.03$) |

## Mean Plasma Levels - Extended Results

| Comparisons | Conditions | Results |
|---|---|---|
| MicroActive® vs Solubilized | 1 week 60 mg 20 Ss | 204% better* |
| | 2 week 60 mg 20 Ss | 187% better ($p<0.002$) |
| | 3 week 60 mg 20 Ss | 170% better ($p<0.03$) |

**not statistically significant***

## Extended Release Results (tmax to 24 hr)

| Comparisons | Conditions | Results |
|---|---|---|
| MicroActive® vs Crystalline | 24 hr 180 mg 8 Ss | 230% better ($p<0.005$) |
| MicroActive® vs Solubilized | 24 hr 180 mg 5 Ss | 42% better ($p<0.002$) |
| MicroActive® vs Solubilized | 24 hr 60 mg 20 Ss | 250% ($p<0.04$) |

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As the price of CoQ10 falls, marketers try to attract the customer with larger doses even though research has shown that the efficiency of absorption is inversely related to the size of the dose. This market approach renders the more bioavailable and beneficial forms of CoQ10 less desirable, since the cost can be more than two times the cost of the crystalline form.

## Supported Health Claims when Blending

A recent BioActives study demonstrated that blending various ratios of MicroActive® complex to crystalline CoQ10 does not affect the bioavailability of the complex. Consider, for example, two products, each with 100 mg of elemental CoQ10, that can attract customers seeking substantial doses. The first contains 30 mg of CoQ10 complex with 70 mg of crystalline CoQ10 added. The second has 70 mg of CoQ10 complex with 30 mg of crystalline CoQ10 added.

| Sustained Release (30 mg elemental) | Sustained Release (70 mg elemental) |
|---|---|
| • Sustained release over 24 hours<br>• Absorption assurance for everyone | • Sustained release over 24 hours<br>• Absorption assurance for everyone |
| • Clinically proven to have superior bioavailablity<br>• Will increase CoQ10 serum levels faster | • Clinically proven to have superior bioavailablity<br>• Will increase CoQ10 serum levels faster<br>• tests show doubled CoQ10 serum levels in 3 weeks<br>• Clinically proven to reduce hypertension |

**Product Specifications**

- Crystal-free
- CoQ10 complexed with cyclodextrin
- Light yellow free-flowing 60 mesh powder
- 26% CoQ10 concentration
- Stable at room temperature
- Water-dispersible
- Suitable for tablets, capsules, softgels, functional beverages

## Uniform Response Results

| Comparisons | Conditions | |
|---|---|---|
| MicroActive® vs Crystalline | 24 hr 180 mg 8 Ss | 7 MicroActive® subjects double plasma level over baseline / 0 Crystalline ($p<0.01$) |
| MicroActive® vs Solubilized | 3 weeks 60 mg 20 Ss | 100% double plasma level over baseline vs 44% solubilized ($p<0.008$) |
| MicroActive® vs Solubilized | 24 hr 60 m-g 20 Ss | Number of subjects with AUC above 12 mg MicroActive®: 5; Softgel: 1; Crystaline: 0 ($p<004$) |
| MicroActive® vs Solubilized | 24 hr 180 mg 5 Ss | Variance in uptake 4.1x more for solubilized ($p<0.003$) |

## Frequently Asked Questions: MicroActive® CoQ10

**Q: What does "assured bioavailability" mean?** Many advanced CoQ10 products claim to be "more bioavailable" by demonstrating improved uptake for a group of subjects. The problem is that within this group some subjects are naturally "super" absorbers, while others still show poor uptake. In contrast, MicroActive® CoQ10 demonstrates superior absorption in all subjects, not just a few. This is why all subjects in the three-week study doubled their CoQ10 levels, compared with the control group in which only 44% of subjects doubled their CoQ10 levels.

**Q: What are cyclodextrins and are they safe?** Natural cyclodextrins are special excipients made from starch, and are used extensively in foods to mask taste, and in pharmaceuticals to facilitate uniform uptake. The ß-cyclodextrin used in MicroActive® CoQ10 is self-affirmed GRAS by the FDA and non-GMO.

**Q: Why are cyclodextrins used in the manufacturing of MicroActive® CoQ10?** Natural cyclodextrins serve two important roles in improving the bioavailability of MicroActive® CoQ10. Each molecule of CoQ10 is joined with two cyclodextrin molecules, forming a complex. In the process of forming the complex, CoQ10 is reduced to its molecular size. The CoQ10 molecules are then prevented from reaggregating because the cyclodextrin in the complex keeps them separated, making the MicroActive® CoQ10 micronized.

The second benefit derived from cyclodextrins is that they render the hydrophobic CoQ10 molecule water-dispersible. This happens because the CoQ10 enters the hydrophobic cavity in the cyclodextrin molecule. The outer surface of the cyclodextrin is hydrophilic, which makes the molecule water soluble/dispersible. Thus the complex of the two becomes water soluble and more easily transported to the absorption site in the small intestines.

**Q: How were the sample sizes and doses determined for the clinical trials?** The sample sizes and doses were selected to be consistent with other published studies on CoQ10 uptake. The studies were reviewed by the Ethical Review Committee (an IRB) who stated:

> The results of the provided data were found to be an acceptable determination that the uptake values were different between the products... that the design and conclusion drawn about bioavailability appear to be consistent with those in other nutritional supplement
> studies appearing in peer reviewed journals"

**Q: What is the unique technological process and is it protected by patents?** The process and benefits of making cyclodextrin complexes are well-known. However, there is an inherent unpredictability issue in cyclodextrin chemistry and its resulting benefits, which is solved in BioActives' patents. For example, γ-cyclodextrin can be complexed with CoQ10, but the result is a product that is less bioavailable than that which uses β-cyclodextrin. The method of drying the complex also contributes to its bioavailability, thus producing an optimal result.

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