

**Lonza**



# L-Carnitine and Coenzyme Q<sub>10</sub>

Supporting Heart Health



Maintaining heart health should be a top priority for us all and fortunately, there's a lot we can do to keep our hearts healthy, including eating a healthy diet, maintaining ideal body weight and exercising regularly. Scientific evidence also suggests that the use of the dietary supplements, L-Carnitine and Coenzyme Q<sub>10</sub> (CoQ<sub>10</sub>), may also support healthy heart function. Let's find out some more...

### What are L-Carnitine and CoQ<sub>10</sub>?

L-Carnitine is an amino acid-like substance, first discovered in meat extracts in 1905. Experts consider CoQ<sub>10</sub> to be a vitamin-like substance and CoQ<sub>10</sub> was first isolated from beef heart mitochondria in 1957<sup>1</sup>.

### Naturally Produced in the Human Body

Both L-Carnitine and CoQ<sub>10</sub> can be made and stored in the human body. L-Carnitine is produced predominantly in the liver and kidney from a number of nutrients, including the essential amino acids lysine and methionine, as well as iron, niacin, vitamins B6 and C. A diet limited in any of these nutrients may impair the ability of the body to synthesize L-Carnitine<sup>2</sup>. While the majority of L-Carnitine in the body is stored in skeletal muscle, the heart also contains a high concentration. The adult human body is estimated to contain 20 - 25 g of L-Carnitine.

CoQ<sub>10</sub> can be synthesized in all tissues and biosynthesis from the amino acid tyrosine is a multistage process requiring at least eight vitamins and several trace elements<sup>1</sup>. CoQ<sub>10</sub> is naturally present in humans with high concentrations in the heart, liver, kidneys and pancreas. Total body content of CoQ<sub>10</sub> is estimated to be 0.5 - 1.5 g<sup>3</sup>.

### Dietary Sources

L-Carnitine and CoQ<sub>10</sub> are both present in certain foods. The richest food sources of L-Carnitine include animal products, such as lamb, beef and pork. Fruits and vegetables contain very little, if any, L-Carnitine. The average non-vegetarian diet is estimated to provide 100 – 300 mg L-Carnitine/day.

CoQ<sub>10</sub> rich foods are mainly meat, poultry and fish. Other rich sources are certain vegetable oils and nuts. Fruits, vegetables, eggs, dairy products and cereals are all moderate sources of CoQ<sub>10</sub>. Most individuals are thought to have a dietary intake of below 10 mg CoQ<sub>10</sub> per day<sup>4</sup>.



### Key Role: Energizing the Body

The body uses carbohydrate, fat and protein consumed daily in food to provide the energy necessary to maintain cellular activities at rest and during exercise<sup>5</sup>. The biochemical and metabolic roles of L-Carnitine and CoQ<sub>10</sub> are closely related and involve facilitating energy production in the body.

L-Carnitine plays a fundamental part in ensuring the production of energy from fat. Fatty acid breakdown ( $\beta$ -oxidation) and subsequent energy production occur inside the mitochondria of the human cell (Figure 1). The mitochondrion is frequently referred to as the "furnace" of the cell, since this is where energy is produced. In order to produce energy from fat, long chain fatty acids need to move into the mitochondria. However, the mitochondrial membrane acts as a barrier to long chain fatty acids, refusing permission to enter. This is where L-Carnitine comes into play. L-Carnitine binds to the long chain fatty acids and through a series of enzymatic steps, it "shuttles" the fatty acids into the mitochondria where they can be subsequently broken down and energy can be produced in the form of adenosine triphosphate, ATP. Thus, to reiterate, L-Carnitine facilitates the production of energy from fat.

**Take Note! L-Carnitine and CoQ<sub>10</sub> both have a vital interrelated role in producing energy in the body: L-Carnitine delivers the fuel (fatty acids) and CoQ<sub>10</sub> helps to make sure energy (ATP), essential for life, is subsequently produced.**

CoQ<sub>10</sub> also has a critical function in the energy-producing process in the body. In humans, the aerobic (meaning in presence of oxygen) production of ATP occurs inside the mitochondria and this process may conveniently be broken into three stages. Stage 1 is the generation of Acetyl-CoA from the products of protein, carbohydrate and fat breakdown, i.e., amino acids, pyruvate and fatty acids, respectively. Stage 2 is Krebs cycle where the Acetyl CoA is broken down and finally, Stage 3 is the process of oxidative phosphorylation (i.e., ATP or energy formation) in the electron transport chain (Figure 1). CoQ<sub>10</sub> acts as an electron carrier in the mitochondrial electron transport chain and thereby plays a critical role in energy production in the body. Circumstances which change the quantity of CoQ<sub>10</sub> in the inner mitochondrial membrane correspondingly change the electron transport rate, thus influencing the efficacy of energy production<sup>6</sup>.

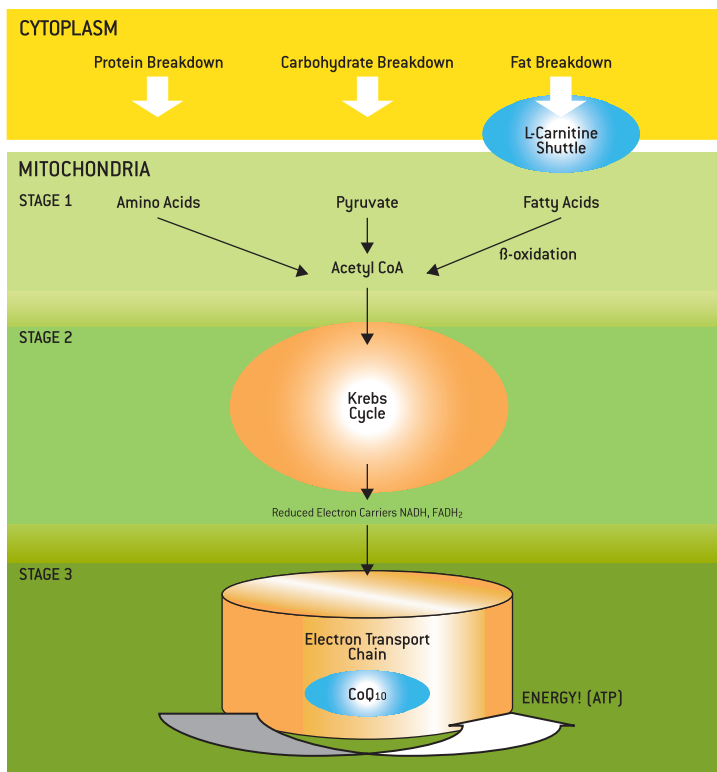


Figure 1: Aerobic Production of Energy. Note the essential involvement of L-Carnitine and Coenzyme Q<sub>10</sub> in this process. (Adapted from reference 5.)

## L-Carnitine and CoQ<sub>10</sub>: Supporting Cardiovascular Health

Following decades of clinical research, L-Carnitine and CoQ<sub>10</sub> are both individually recognized as key supplements for supporting cardiovascular health. The heart actually depends upon L-Carnitine for most of its energy production because the majority of the heart's energy supply comes from the breakdown of fat<sup>7</sup>. Recall that L-Carnitine's role in the body is in ensuring the production of energy from fat.

A brief insight into cardiovascular disease may be helpful before further discussion. Similar to any other tissue, the heart muscle must receive oxygen-rich blood in order to function efficiently. The coronary arteries are the blood vessels responsible for supplying this blood to the heart muscle. Coronary artery disease is a condition in which fatty deposits accumulate in the walls of the coronary arteries and obstruct blood flow to the heart muscle. As the obstruction gets bigger, it causes inadequate blood flow (ischemia) to the heart muscle and this, in turn, can cause heart damage. Coronary artery disease can ultimately lead to angina, a heart attack and heart failure<sup>8</sup>.

**Although L-Carnitine and CoQ<sub>10</sub> are typically marketed as dietary supplements and the U.S. Food and Drug Administration therefore restricts claims to those associated with supporting a healthy cardiovascular system, studies conducted on L-Carnitine's and CoQ<sub>10</sub>'s role in the management of cardiovascular conditions provide substantiation in support of dietary supplement claims. Discussions of these studies are solely intended to describe the substantiation underlying dietary supplement claims and are not intended to state or imply an intended use of L-Carnitine and CoQ<sub>10</sub> dietary supplement products for these conditions. Consultation with a healthcare practitioner is advisable for individuals with these conditions to determine which products are appropriate.**



## L-Carnitine, CoQ<sub>10</sub> and Angina

Angina is the temporary chest pain that occurs while the heart muscle is not receiving enough oxygen (via the blood). Usually, angina is caused by coronary artery disease<sup>8</sup>. In stable angina, individuals have episodes of chest pain that are predictable and usually occur on physical exertion or under mental or emotional stress<sup>9</sup>. In stable angina, the ability to exercise is usually diminished because of the onset of chest pain. Complications include the development of unstable angina, a heart attack or fatal irregular heart rhythms<sup>10</sup>. In 2001, it was estimated that almost 7 million Americans had angina<sup>9</sup>.

### Clinical Research Findings in Support of Dietary Supplement Claims

Numerous clinical studies document the positive effects of L-Carnitine in people with stable angina<sup>11-14</sup>. In one study, 200 people with stable angina were divided into a control group and an L-Carnitine group who were supplemented with 2g L-Carnitine/day for 6 months, in addition to their routine drug treatment. Supplementation with L-Carnitine was associated with significantly improved exercise tolerance, improved heart function and performance, reduced need for cardioactive drugs and significantly improved blood lipid (cholesterol and triglyceride) levels<sup>15</sup>.

A number of small clinical studies also suggest that CoQ<sub>10</sub> supplementation can be beneficial for people with stable angina<sup>16</sup>. In one study, 12 people with stable angina were given CoQ<sub>10</sub> (150 mg/day) or placebo for 4 weeks in a double-blind, placebo-controlled, crossover study. CoQ<sub>10</sub> supplementation was associated with a significant increase in exercise tolerance, as well as reduced incidence of anginal attacks and need for angina-relieving medication<sup>17</sup>.

## L-Carnitine, CoQ<sub>10</sub> and Heart Attack (Myocardial Infarction)

A heart attack occurs when the blood supply to part of the heart muscle is severely reduced or completely cut-off, usually as a result of the build-up of fat deposits in the coronary arteries. If the blood supply to the heart muscle is cut-off for more than a few minutes, muscle cells suffer permanent injury and die<sup>9</sup>. The extent of heart muscle damage dictates the overall outcome for the person having the heart attack. If more than half of the heart muscle is damaged, the heart generally cannot function and death or disability is likely<sup>8</sup>. In 2004, it is estimated that 700,000 Americans will have a new heart attack, while a further 500,000 will have a recurrent attack<sup>9</sup>.

### Clinical Research Findings in Support of Dietary Supplement Claims

L-Carnitine supplementation has been shown to be beneficial in supporting heart function in people who have had a recent heart attack<sup>18</sup>. In a 12 month study, 160 people who had a recent heart attack were divided into two groups: a control group (routine pharmacological therapy) and an L-Carnitine group (routine pharmacological therapy plus 4g L-Carnitine/day). It was observed that L-Carnitine exerted cardioprotective effects by improving heart rate, decreasing complications (such as angina and arrhythmias) and most importantly, by significantly reducing the rate of mortality (Figure 2)<sup>19</sup>. In addition to reducing complications such as angina and irregular heartbeats, supplementing with L-Carnitine (2g/day for 28 days) following a recent heart attack may be protective by reducing the extent of damage to the heart muscle<sup>20</sup>.

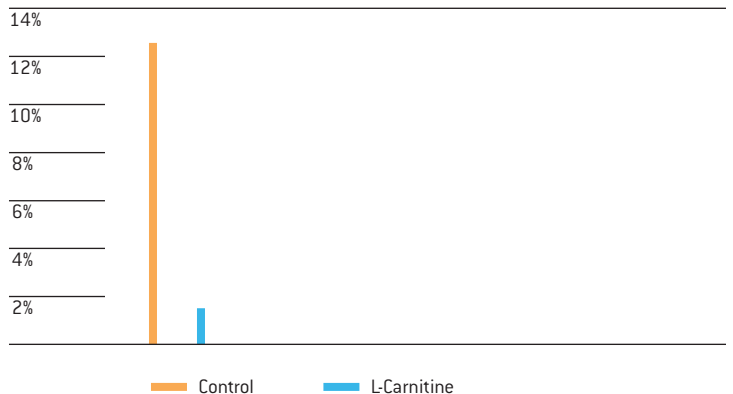


Figure 2: Rate of mortality in post-heart attack subjects following treatment with L-Carnitine (4g/day for 12 months)<sup>19</sup>.



Preliminary clinical research indicates that CoQ<sub>10</sub> supplementation positively supports heart function in people who have had a recent heart attack. In a double-blind, placebo-controlled study, 144 people who had a very recent heart attack were assigned to either a CoQ<sub>10</sub> group (120 mg/day for 28 days) or a placebo (B vitamin) group. Routine pharmacological therapy was also taken by both groups. After 28 days, angina, irregular heartbeats and signs of cardiac dysfunction were significantly reduced in the CoQ<sub>10</sub> group, as compared to the placebo group. In addition, indicators of free radical stress and cell damage due to the heart attack were significantly reduced in the CoQ<sub>10</sub> group, while plasma levels of the antioxidant vitamins A, E, C and beta-carotene were significantly elevated<sup>21</sup>. At the 1 year follow-up, it was reported that plasma levels of Vitamin E and C were significantly elevated in the CoQ<sub>10</sub> group, while markers of free radical stress and cell damage were significantly reduced. Subjects given CoQ<sub>10</sub> also showed a significant reduction in total and LDL-cholesterol and a significant increase in HDL-cholesterol (the “healthy” cholesterol). Total cardiac events were significantly reduced in the CoQ<sub>10</sub> group (24.6%) as compared to the placebo group (45.0%)<sup>22</sup>.

### L-Carnitine, CoQ<sub>10</sub> and Heart Failure

Heart failure is a serious condition in which the quantity of blood pumped by the heart each minute is insufficient to meet the body’s needs for oxygen and nutrients. As a result, people with heart failure tend to feel weak, fatigued or short of breath. The most common cause is coronary artery disease<sup>9</sup>. Other causes include a previous heart attack, high blood pressure, diabetes and heart muscle disease (cardiomyopathy). The New York Heart Association (NYHA) Functional Classification places people with heart failure in categories I through IV depending upon how limited they are during physical activity. Class I indicates the mildest, and class IV the most severe, form of heart failure. In 2001, about 5 million Americans were living with heart failure<sup>9</sup>. About 70% of people with heart failure die of the disease within 10 years<sup>8</sup>.

### Clinical Research Findings in Support of Dietary Supplement Claims

Clinical research has found that L-Carnitine supplementation is of benefit to people with heart failure by supporting heart function and reducing some of the symptoms experienced<sup>23-25</sup>. In a placebo-controlled, randomized, double-blind trial, L-Carnitine supplementation (3g/day for 120 days), in addition to routine pharmacological therapy, was found to significantly improve exercise tolerance and performance in individuals with NYHA Class II and III heart failure. The beneficial effect of the L-Carnitine increased with the duration of supplementation<sup>26</sup>. In a long term clinical study, people with NYHA Class III or IV heart failure were given L-Carnitine (2g/day) or placebo for almost 3 years. The results are exciting in that the researchers reported a significant reduction in mortality rate in the L-Carnitine group (3%) versus the placebo group (18%) who were given standard therapy only<sup>27</sup>.

Many double-blind, placebo-controlled, crossover studies, as well as open trials and large multicenter trials have looked at the effect of CoQ<sub>10</sub> in people with heart failure and the majority of these studies indicate that CoQ<sub>10</sub> supplementation, in addition to conventional drug therapy, positively supports heart function in cardiomyopathy and heart failure<sup>28-33</sup>. In a double-blind, placebo-controlled, crossover trial, 19 people with cardiomyopathy (NYHA Class III or IV) were given placebo or CoQ<sub>10</sub> (100 mg/day) for 12 weeks, in addition to conventional therapy. A significant improvement in cardiac function occurred with CoQ<sub>10</sub> supplementation<sup>34</sup>. In an open, long-term trial, the effect of CoQ<sub>10</sub> supplementation (average 242 mg/day for an average of 17.8 months) was studied in 424 people with heart failure due to various causes. Supplementation was associated with clinical improvement as assessed by NYHA class (Figure 3), a significant improvement in cardiac function, as well as reduced requirement for cardiac medications. It was concluded that CoQ<sub>10</sub> is a safe and effective adjunctive treatment for a broad range of cardiovascular diseases<sup>35</sup>.

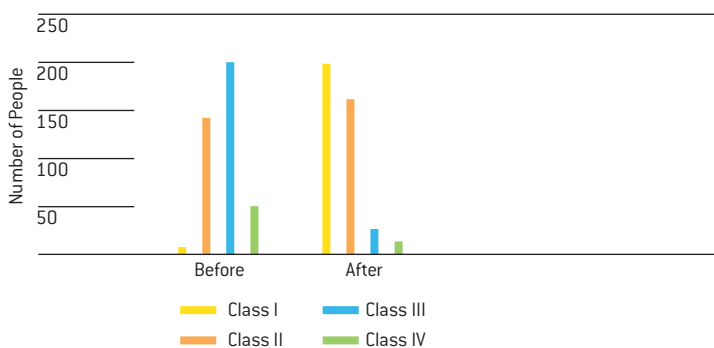


Figure 3: NYHA functional class before and after CoQ<sub>10</sub> supplementation in people with heart failure<sup>35</sup>. Movement to a lower class indicates clinical improvement.



### L-Carnitine: Possible Mechanisms of Action in Supporting Heart Health

The precise mechanism by which supplemental L-Carnitine exerts its action on heart metabolism and function in ischemic heart disease, including angina and heart attack, is not very well understood. An obstructed coronary artery leads to inadequate blood flow (oxygen supply) to the heart muscle. This, in turn, causes a reduction in fatty acid breakdown in the area of the heart supplied by the narrowed coronary artery. In addition, a loss of free L-Carnitine occurs which further reduces the capacity for fatty acid breakdown. The reduction in fatty acid breakdown, in turn, leads to the production of damaging metabolites which can ultimately slow down energy production and impair metabolic and mechanical function in the heart. Scientists propose that supplemental L-Carnitine is beneficial under these conditions by helping to restore free L-Carnitine concentrations, promoting fatty acid breakdown and energy production and by acting as a scavenger of the damaging metabolites<sup>36</sup>. Similarly, in heart failure, there is a decrease in L-Carnitine in the heart tissue and L-Carnitine supplementation helps restore fatty acid oxidation and energy production in the energy starved heart<sup>24</sup>.

### CoQ<sub>10</sub>: Possible Mechanisms of Action in Supporting Heart Health

The mechanism by which CoQ<sub>10</sub> promotes increased exercise tolerance in people with angina is poorly understood. Possibly, CoQ<sub>10</sub>'s anti-anginal action results either from enhanced resynthesis of ATP (energy), a direct membrane protection mechanism or through the reduction of damaging free radical species<sup>3</sup>. Following a heart attack, CoQ<sub>10</sub> supplementation appears to significantly reduce the risk of further cardiac events. This is possibly due to CoQ<sub>10</sub>'s rapid protective effect on thrombosis (clot formation), endothelial function, oxidative damage, as well as vascular and myocardial remodeling. The observed decrease in markers of free radical stress and cell damage and increase in plasma

levels of Vitamin E in post-heart attack subjects supplemented with CoQ<sub>10</sub> may be attributed to the established antioxidant and Vitamin E-sparing properties of CoQ<sub>10</sub><sup>22</sup>. In the case of heart failure and cardiomyopathy, CoQ<sub>10</sub> supplementation is thought to correct the observed deficiency of CoQ<sub>10</sub> in the heart, resulting in improved energy production which supports cardiac function<sup>34</sup>.

### Combining L-Carnitine and CoQ<sub>10</sub> to Support Heart Health

Clearly, on an individual basis, L-Carnitine and CoQ<sub>10</sub> have an important role to play in supporting and maintaining heart health. Both have inter-related functions in energy production in the body. On this basis, it seems reasonable to suggest that combining L-Carnitine with CoQ<sub>10</sub> for supporting heart health might have an additive protective effect for the heart. Animal studies have documented the cardioprotective benefits of combining L-Carnitine and CoQ<sub>10</sub><sup>37</sup>. Notably, in rats fed a high cholesterol diet for 6 weeks, the incidence of atherosclerosis (build up of fatty deposits in arteries which leads to heart disease) was lower when the rats had both CoQ<sub>10</sub> and L-Carnitine added to the diet<sup>38</sup>.

**Take Note! In the US, L-Carnitine and CoQ<sub>10</sub> are available as stand-alone dietary supplement products or as combination products containing both L-Carnitine and CoQ<sub>10</sub>. Lonza, the leading supplier of L-Carnitine to the dietary supplement industry, is pleased to provide high quality L-CARNIPURE® L-Carnitine to dietary supplement manufacturers wishing to produce energizing and heart healthy L-Carnitine and CoQ<sub>10</sub> combination products.**

### Supplementation, Safety and Side Effects

L-Carnitine and CoQ<sub>10</sub> supplementation may be advisable for people concerned with maintaining everyday energy levels and supporting a healthy heart. Although symptoms of heart disease may not start to appear until middle age or older, scientists have found that heart disease begins developing well before this. Therefore, making good lifestyle

choices such as eating healthy foods and exercising regularly is important earlier in life. Taking L-Carnitine and CoQ<sub>10</sub> may offer further cardioprotection. It is also worth noting that as we age, the levels of both L-Carnitine and CoQ<sub>10</sub> decrease in the body. More than ever, at this time in the life cycle, maintaining energy levels and heart health is essential for good quality of life.

Based on the numerous clinical studies conducted to date, it appears that both L-Carnitine and CoQ<sub>10</sub> are very safe with few side effects reported. **Scientific literature has documented an interaction between CoQ<sub>10</sub> and certain drugs, making consultation with a physician advisable before supplementation.**

## Lonza – The Leader in L-Carnitine

Lonza is the world's leading supplier of pharmaceutical grade L-CARNIPURE® L-Carnitine bulk products to the dietary supplement, pharmaceutical and infant formula industries.

Lonza's L-CARNIPURE® L-Carnitine products include:

- L-Carnitine Crystalline
- L-Carnitine L-Tartrate (US patent 5,073,376, Japanese patent 2,546,068 and other international patents)
- L-Carnitine Magnesium Citrate (US patent 5,071,874 and other international patents)
- Acetyl-L-Carnitine

L-CARNIPURE® L-Carnitine L-Tartrate is the most popular form of L-Carnitine in the marketplace. This white, crystalline, free-flowing, non-hygroscopic form of L-Carnitine is ideally suited for tablets and capsules (both hard-shell and soft-gel), as well as liquid applications. Of all stable L-Carnitine salts commercially available, L-Carnitine L-Tartrate has the highest content of L-Carnitine (68%), with 32% natural L-Tartaric Acid. L-CARNIPURE® L-Carnitine L-Tartrate and L-Carnitine Crystalline are Generally Recognized as Safe and are Kosher and OU certified.

With quality assurance of utmost importance, Lonza's L-CARNIPURE® L-Carnitine products are:

- manufactured using a unique patented production process
- produced in a state-of-the-art, FDA registered and ISO 9001:2000 certified plant
- manufactured in compliance with current Good Manufacturing Practice
- free from animal products and genetically modified organisms (GMOs)
- free from any harmful D-Carnitine, hence the quality assurance logo, L-CARNIPURE®.



Current Product Information Sheets for Lonza's L-CARNIPURE® L-Carnitine products are available at [www.carnitine.com](http://www.carnitine.com).

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