

Carnipure™ Focus

Cardiovascular health

Lonza

Introduction

The contribution of L-Carnitine to a healthy cardiovascular system has a long and established history and forms the largest part of all publications on L-Carnitine¹. The term cardiovascular system is often used in the press when it comes to the discussion about health conditions around the heart. But what does cardiovascular system mean exactly? “Cardio” means heart and “vascular” means blood vessels. Hence, the circulatory system of the heart and blood vessels is the cardiovascular system². With this explanation, it is easy to understand that a healthy heart is also accompanied by healthy blood vessels. In this context nutrition has assumed a prominent role for both the prevention and treatment of cardiovascular disease³. This includes the daily supply of a balanced diet with carbohydrates, fat, and proteins as well as vitamins, minerals and of course L-Carnitine. Furthermore a regular exercise program, stress reduction, a non-smoking lifestyle and only moderate alcohol consumption additionally support healthy cardiovascular conditions.

The importance of a healthy cardiovascular system

A healthy and well-balanced lifestyle is a worthwhile investment. This becomes clear immediately with a more detailed look at the causes of deaths worldwide. According to estimates from the World Health Organization (WHO) cardiovascular diseases were the number one cause of death globally in 2005⁴.



Some more heart facts^{4,5}

Cardiovascular diseases (CVD) mostly affect people in their peak mid-life.

One in three female adults is affected by cardiovascular disease. Since 1984, the number of CVD deaths of females has exceeded those of males

The estimated direct and indirect cost of CVD in the United States for 2008 is \$ 448.5 billion.

The WHO predicts 11.0 million deaths from coronary heart disease in the year 2020.

What is Carnipure™?

Carnipure™ is high quality L-Carnitine manufactured by the Swiss life-science company Lonza. L-Carnitine is a nutrient that plays an important role in energy metabolism. The proprietary Carnipure™ production process was invented by Lonza scientists in Switzerland. It directly produces the L-isomer of Carnitine, the beneficial form found in nature. Products displaying the Carnipure™ quality seal on the packaging show the consumer that they contain pure L-Carnitine from Lonza.



Carnipure™ offers purest L-Carnitine and is a trademark of Lonza Ltd, Switzerland.

What is Carnitine?

L-Carnitine is a natural and safe nutrient which gives everybody an adequate chance to keep the heart and vessels healthy. This applies for people with risk factors who have not yet developed clinical manifest cardiovascular diseases (primary prevention) as well as people with established coronary heart diseases (secondary prevention).

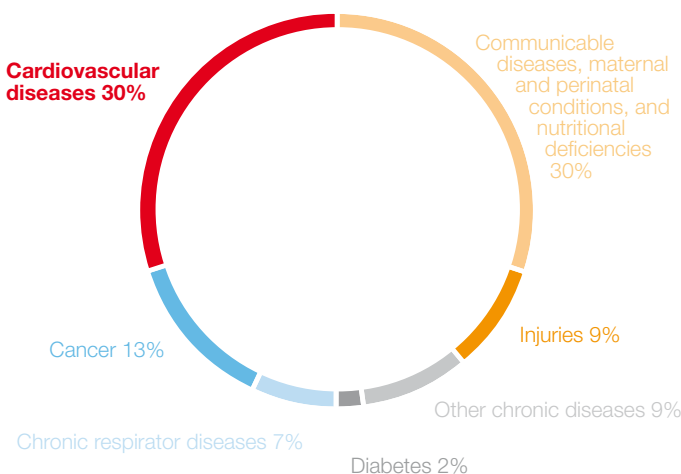


Figure 1: Cardiovascular diseases were the number one cause of death globally in 2005⁴

L-Carnitine is for humans an essential co-factor for the transport of long-chain fatty acids across the inner mitochondrial membrane into the matrix, where they are broken down for energy production (β -oxidation)⁶.

In humans with a normal omnivore diet approximately 75 per cent of the L-Carnitine intake comes from dietary sources. In particular animal products such as meat, poultry, fish, and dairy products provide the L-Carnitine obtained from mixed diets. The remaining L-Carnitine (approx. 25 per cent) is synthesized by the human body predominantly in the liver, kidney and brain from the essential amino acids lysine and methionine in the presence of vitamin B6, vitamin C, niacin, and iron. The ingested and synthesized L-Carnitine is carried for storage via blood, predominantly in heart and skeletal muscles⁷. It has been shown, however, that in the last decade in Europe the average dietary L-Carnitine intake has decreased by 20% as a result of decreased meat consumption^{8, 9}.

L-Carnitine in the Heart

A proper heart function relies on high efficiency of energy conversion in which L-Carnitine is directly involved. In the healthy adult heart muscle the fatty acid oxidation accounts for most of the energy generation with a little contribution of glucose and under, certain circumstances, also substrates such as lactate, ketone bodies, and amino acids^{10, 11}.

The heart has a small capacity for both the synthesis and storage of fatty acids. Therefore, the heart relies mainly on the fatty acid supply from the blood. Before the breakdown of these long chain fatty acids takes place inside the mitochondria, they have to be transported across the mitochondrial membrane. Now, L-Carnitine comes into play because of its function to carry these free fatty acids across the mitochondria membrane for the β -oxidation.

Due to this fact, it is not surprising that the L-Carnitine concentration in the heart is the highest in the body. This means that the L-Carnitine concentration in the heart is over three times higher than that in the skeletal muscle, four times higher than in the liver, and eight times higher than that in the kidney. The skeletal and heart muscles lack the potential for synthesizing L-Carnitine. Therefore, the heart is relying on the L-Carnitine supply from the blood. This transport process into the heart cells is in fact a fascinating process because it happens via an active extraction of L-Carnitine from the blood plasma against a 60-fold concentration gradient¹².

Antioxidative effect of L-Carnitine

Atherosclerosis is commonly called hardening of the arteries, which includes a variety of conditions that causes artery walls to thicken and lose elasticity (e.g. free radicals, high cholesterol level).

There is clear evidence that oxidative stress plays an important role in the development of cardiovascular diseases. In contrast, diets rich in antioxidants have been shown to exert protective effects to the atherogenic process and this in turn is also beneficial to a healthy heart¹³.

L-Carnitine has been shown, for example, to have a stimulatory effect on the expression of specific proteins/enzymes (Heme oxygenase-1, Endothelial constitutive nitric oxide synthase) which have antioxidant and anti-inflammatory properties. This means that L-Carnitine might be able to protect from oxidative stress related cardiovascular risk factors and myocardial damage¹⁴.

L-Carnitine has also been described in several other in-vitro and animal studies as an antioxidative substance which has shown to be effective in conditions characterized by increased oxidative stress^{15, 16}. Moreover, in human trials with people who exercise regularly the supplementation of Carnipure™ has supported a reduced accumulation of free radicals which may have a favorable effect on endothelial blood flow regulation^{17, 18}.

Effect of L-Carnitine on cholesterol metabolism

What is cholesterol and where does it come from?

Cholesterol is a soft, fat-like substance. It is found in the blood and in all the body's cells. It is an important part of a healthy body because it is used to form cell membranes, some hormones and other needed tissues. People get cholesterol in two ways: it is synthesized naturally in the body and also comes directly from foods (e.g. egg yolks). However, too much cholesterol in the blood can increase the risk of getting coronary heart disease. Cholesterol has to be transported in the blood by special carriers called lipoproteins – the main ones are²:

- LDL Low density lipoprotein – the “bad one”
- HDL High density lipoprotein – the “good one”

The beneficial effect of L-Carnitine supplementation on the cholesterol level has been shown in some animal studies^{19, 20}. Furthermore, there also exist clinical trials which came to the conclusion that L-Carnitine may have a favorable effect on total cholesterol, LDL- and HDL-cholesterol as well as triglycerides:



The supplementation of 1 g L-Carnitine daily for 90 days resulted in significantly decreased levels of total-, and LDL-cholesterol in 24 males and females with elevated levels of blood lipids. This effect leads to a less atherogenic plasma lipoprotein fatty acid profile in these people²¹. Furthermore, in another study, 84 elderly people (aged from 70-92) with onset of fatigue following slight physical activity received placebo or 2 g L-Carnitine twice daily during the 30-day-study phase. The L-Carnitine-treated group showed at the end of the study significant improvements in the following parameters: total cholesterol (-16%), LDL (-28%), HDL (+19%), triglycerides (-6%) compared with placebo [Figure 2]²².

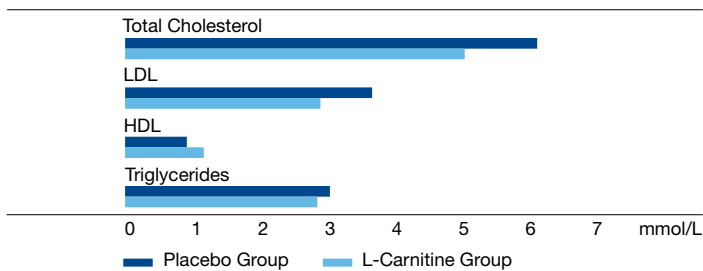


Figure 2: Blood cholesterol and triglyceride values in elderly after 30 days of L-Carnitine supplementation²²

L-Carnitine and heart performance

It has been shown in several experimental models and human clinical trials that an adequate intake of L-Carnitine may have a favorable effect on maintaining a healthy heart and vessels²³. In contrast, there are also studies which came to the result that the failing heart muscle has a low L-Carnitine level^{24, 25}. Therefore L-Carnitine supplementation can be beneficial to the organ by counteracting the toxic effects of free fatty acids and improving carbohydrate metabolism²⁶.

L-Carnitine and exercise tolerance

Angina Pectoris is the medical term for chest pain or discomfort due to coronary heart disease. In this condition, the heart muscle does not get enough blood resulting in chest pain. People with stable angina have episodes of chest discomfort that are usually predictable. They occur with exertion (such as running to catch a bus) or under mental or emotional stress².

It has been found that the addition of L-Carnitine to the regular medical treatment for chronic angina can help to improve exercise tolerance. In a randomized, placebo-controlled trial with 47 men and women with chronic stable angina, the addition of L-Carnitine (2 g/d) in the daily nutrition for three months significantly improved

exercise duration and decreased the time required for exercise induced changes to return to baseline, in comparison to the placebo²⁷. This has also been shown in another study with 200 people with exercise-induced stable angina. The supplementation of 2 g L-Carnitine per day for 6 months in addition to regular medical therapy has led to significantly improved exercise tolerance and improved cardiac function²⁸.

The L-Carnitine supplementation may also improve the exercise tolerance and the muscle metabolism in people with peripheral arterial disease. This is a type of peripheral vascular disease that affects blood circulation, primarily in arteries leading to the legs and feet. It is mainly caused by atherosclerosis. People with peripheral arterial disease are at increased risk of cardiovascular events and come along with reduced exercise performance. L-Carnitine interacts with the skeletal muscle acyl-CoA pool and helps therefore to reduce symptoms²⁹.

A healthy heart function and L-Carnitine

A heart attack is when low blood flow causes the heart to be starved of oxygen. Then parts of the heart muscle die or become permanently damaged. This is called a myocardial infarction. Heart attacks occur most often as a result of a condition when a plaque (deposits of fat-like substances) builds up over many years on the inside walls of the coronary arteries (the arteries that supply blood and oxygen to your heart). Severe problems linked to a heart attack can include heart failure and irregular heartbeats (arrhythmias)².

L-Carnitine can deliver a contribution to a more regular and healthier heart beat in addition to a regular medical treatment after a myocardial infarction has occurred. This could be demonstrated, for example, in a double-blind, placebo-controlled clinical trial with patients who had suffered from a first heart attack. The supplementation of L-Carnitine (2 g/d) for 28 days contributed to a healthier heart function in these people compared to placebo³⁰. Other clinical trials came to the same results^{31, 32}.

And so to conclude

L-Carnitine can be considered as an energy balancing factor in the heart which makes it essential for a proper heart function. This is mainly based on two facts: Firstly, the primary function of L-Carnitine is to transport long-chain fatty acids across the mitochondria membrane for their energy production and secondly, fatty acids are the main substrate for the energy production in the normally functioning heart. Additionally, L-Carnitine is also known to act as a free radical scavenger and may help to maintain adjusted blood lipids such as cholesterol and triglycerides. In conclusion: Carnipure™ supplementation can support a healthy cardiovascular system in different ways with the additional advantage that Carnipure™ has no side effects.

Note: This document is an overview of published scientific information on L-Carnitine and published scientific information on clinical and nutritional trials with L-Carnitine and its derivatives. No claims are made herein for any particular consumer product, nor can these statements be used on such consumer products. The recommended use for Carnipure™ is as a nutrient or dietary supplement.

The statements in this document have not been evaluated by any Food and Drug Administration. Lonza's Carnipure™ is not intended to diagnose, treat, cure or prevent any disease.

No statement is intended or should be construed as a recommendation to infringe any existing patent. The information contained herein is believed to be correct and corresponds to the latest state of scientific and technical knowledge.



References

1. Löster H (2007). Carnitin und seine Bedeutung bei kardiovaskulären Erkrankungen. Ponte Press Verlags-GmbH Bochum
2. American Heart Association (2008). [URL: www.americanheart.org]
3. Katcher HI et al. (2006). In: Present Knowledge in Nutrition. (Edt. Bowman BA, Russell RM). 9th Edition, ILSI press, Washington, DC
4. World Health Organization, WHO (2008). [URL: www.who.int/chp]
5. Wayne R et al. (2008). Circulation 117: e25 – e146
6. Steiber A et al. (2004). Molecular Aspects of Medicine 25 (5-6): 455–473
7. Löhniger et al. (2005). Monatsheft für Chemie 136: 1255–1268
8. FAO Food Supply (2000). [URL: www.fao.org]
9. Knüttel-Gustavsen S & Harmeyer J (2007). Food Chem 86 (1): 137–142
10. Kodde IF et al. (2007). Comparative Biochemistry and Physiology, Part A 146: 26–39
11. Carvajal K & Moreno-Sánchez R (2003). Archives of Medical Research 34: 89–99
12. Lango R et al. (2001). Cardiovascular Research 51: 21–29
13. Hornstra G et al. (1998). Brit J Nutr 80 (Suppl. 1): S113–146
14. Calò LA et al. (2006). Inter J Cardiol 107 (1): 54–60
15. Gülçin I (2005). Life Sciences 78 (5): 803–811
16. Gómez-Amores L et al. (2007). J Nutr Biochem 18 (8): 533–540
17. Spiering BA et al. (2007). Journal of Strength and Conditioning Research 21 (1): 259–264
18. Volek JS et al. (2002). Am J Physiol Endocrinol Metab 282: E474–E482
19. Sayed-Ahmed MM et al. (2001). Pharm Res 44 (3): 235–242
20. Diaz M et al. (2000). Lipids 35 (6): 627–632
21. Stefanutti C et al. (1998). Clin Ter 149 (2): 115–119
22. Pistone G et al. (2003). Drugs Aging 20 (10): 761–767
23. Kendler BS (2006). Journal of Cardiovascular Nursing 21 (1): 9–16
24. Baker H et al. (2005). Nutrition 21: 348–350
25. Regitz V et al. (1990). Am J Cardiol 65: 755–760
26. Hoppel C (2003). Am J Kidney Dis 41 (4): Suppl.4, S4–S12
27. Iyer RN et al. (2000). J Assoc Physicians India 48 (11): 1050–1052
28. Cacciatore L et al. (1991). Drugs Exptl Clin Res XVII (4): 225–335
29. Hiatt WR (2004). Ann NY Acad Sci 1033: 92–98
30. Singh RB et al. (1996). Postgrad Med J (72): 45–50
31. Iliceto S et al. (1995). J Am Coll Cardiol 26 (2): 380–387
32. Davini et al. (1992). Drugs Exptl Clin Res XVIII (8): 355–365

For more information:

Worldwide

Lonza Ltd, Basel, Switzerland

Tel +41 61 316 81 11

In the USA

Lonza Inc, Allendale, NJ

Tel +1 800 365 8324

carnipure@lonza.com

www.carnipure.com

www.lonzanutrition.com.



Carnipure™ offers purest L-Carnitine and is a trademark of Lonza Ltd, Switzerland.