

# Carnipure™ Focus

## Healthy Aging

Lonza

### Introduction

Although philosophers and scientists have long been interested in the aging process, general interest in this fascinating and highly important topic was minimal before the 1960s. In recent decades, however, interest in aging has greatly accelerated. According to the WHO, both the number and the proportion of older persons – defined as aged 60 and over – are growing in virtually all countries<sup>1</sup>. Japan doubled its percent of population age 65 or older in just 26 years, but aging is occurring even more rapidly in Brazil, Singapore, and Thailand<sup>2</sup>. Present worldwide trends are likely to continue unabated. Today, there are an estimated 580 million elderly people in the world, whereas by 2025, this figure is expected to rise to 1000 million. In the developed world, the very old (age 80+) is the fastest growing population group<sup>1</sup>.



### What is Carnipure™?

Carnipure™ is a special grade of L-Carnitine, manufactured by the Swiss life sciences company Lonza. Thanks to a unique production process based on fermentation, Lonza is the only L-Carnitine manufacturer capable of producing L-Carnitine in the same way as nature. Products carrying the Carnipure™ quality seal on the packaging show the consumer that they contain pure Lonza L-Carnitine.



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

Maintaining good quality of life as we age is important. Carnipure™ is the supplement of choice to help maintain good health. For the major part, the daily L-Carnitine requirements are met by food intake. Foods of animal origin are rich in this nutrient, whereas plant foods contain very little, if any, L-Carnitine. An average non-vegetarian diet is estimated to provide 100–300 mg L-Carnitine per day. Small quantities of L-Carnitine are synthesised in the human body. Endogenous synthesis requires six nutrients, including amino acids (lysine and methionine), vitamins C and B6, niacin and iron<sup>3</sup>.

### What happens in the body when we get old?

Clinically, aging is the progressive accumulation of changes occurring in an organism which ultimately lead to death<sup>4</sup>. Numerous aging theories have been proposed. Although it is abundantly clear that our genes influence aging and longevity, exactly how this takes place on a chemical level is only partially understood<sup>5</sup>. Oxygen radicals are increasingly discussed as an important factor involved in the phenomenon of biological aging of all the tissues in the body<sup>6</sup>. The survival of an organism may depend on its ability to overcome the toxic effects of free radicals.

The body's cells use oxygen in metabolic reactions. In this process, oxygen sometimes reacts with body compounds and produces highly unstable molecules known as free radicals. In addition to normal body processes, environmental factors such as radiation, pollution, tobacco smoke, and a high-fat diet generate free radicals. Free radicals can lead to widespread damage as they attack polyunsaturated fatty acids in cell membranes and alter functions of cell proteins and their DNA, creating mutations<sup>7</sup>.

The body contains a couple of lines of defense against free radical damage. The major antioxidative defense system in the body includes scavengers such as glutathione, vitamin C, vitamin E and antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase<sup>8</sup>.

According to Dr. Bruce Ames from the University of California, USA, the mitochondria are the “weak link in aging”<sup>9</sup>. Their function decreases largely with age<sup>7</sup>. Deterioration of mitochondria is implicated in aging and a variety of age-related diseases<sup>10</sup>. The mitochondrion, also referred to as the “furnace of the cell”, is the place of fatty acid and glucose breakdown and ultimate energy generation. In these processes, L-Carnitine plays a major role. It shuttles the long chain fatty acids through the inner mitochondrial membrane<sup>11</sup>. Furthermore, it supports the availability of free Coenzyme A. Accumulating acetyl moieties are transferred from Coenzyme A to L-Carnitine.

Elderly people have a lower energy demand and eating habits change with age<sup>1, 12</sup>. For example, they usually consume less meat. At the same time, the dietary intake of both L-Carnitine and the nutrients required to make L-Carnitine is reduced. A decreased endogenous synthesis could also be shown by researchers<sup>13</sup>. A decrease of L-Carnitine in various body compartments with age has often been described in literature<sup>14, 15</sup>. The resulting reduction in energy metabolism due to lower L-Carnitine levels can be restored

by L-Carnitine supplementation. Two months of Carnipure™ tartrate administration (2 g/d) was shown to partly reverse age-related changes of oxidative metabolism in elderly females<sup>16</sup>.

## L-Carnitine and Brain Function

Aging induces several structural and functional changes in the brain<sup>17</sup>. Blood supply to the brain decreases with age. The number of neurons, the brain cells that specialize in transmitting information, diminishes. An imbalance of changes caused by increased production of free radicals and decreased functional efficiency of the antioxidant system has been suggested to be one of the primary factors that contribute to the aging process<sup>18</sup>. The reason why the brain is prone to oxidative damage lies in its comparatively high level of oxygen metabolism and the unique composition of its cellular membrane that contains large amounts of oxygen-sensitive polyunsaturated fatty acids. Peroxidation of membrane lipids makes the mitochondria membrane more permeable, which leads to a decline in ATP synthesis<sup>19</sup>. Memory loss is accompanied, but not necessarily caused, by accumulation of oxidative damage to lipids, proteins and nucleic acids, and by mitochondrial decay, all of which can disrupt neuronal function.

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Transmitters that conduct messages between parts of the nervous system are called neurotransmitters. They control the other organs by sending impulses through neurons. The neurotransmitter acetylcholine, for example, is responsible for control of blood pressure, gut tone and secretion of glands, among others. It is released into the synaptic slot after excitation and hydrolysed there very quickly by the enzyme acetylcholinesterase. The activity of this enzyme in the brain decreases with age. Loss of enzyme activity may indicate functional decline in the nerve cells.

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Several animal studies suggest that L-Carnitine supplementation could support brain functions. It was found to suppress seizures and impairments of brain metabolism caused by hyperammonaemia in mice<sup>20</sup>. This effect is attributed to an increase in the rate of urea production in the liver by L-Carnitine supplementation. Thus nitrogen is excreted and does not accumulate as ammonia in the blood.

Administration of L-Carnitine to old rats for up to 21 days reversed the age-associated changes in lipid peroxidation and enzymatic antioxidants in various brain regions in a duration-dependent manner<sup>21</sup>. Also, the levels of non-enzymatic antioxidants such as glutathione, vitamin C and vitamin E in old rats were found to be restored by L-Carnitine supplementation. Results suggest that the neuroprotective effect on the brains of old rats was achieved by the elevation of antioxidants with L-Carnitine, and L-Carnitine administration was found to prevent age-related increment on DNA damage<sup>17, 22</sup>. It is noteworthy that similar results were obtained when

repeating these analyses in other organs such as blood, liver and kidney tissue of old rats<sup>10, 23, 24</sup>.

Age-related decline in cholinergic function is thought to be partially responsible for short-term memory disorders during senescence. Also in Alzheimer's disease, there is a consistent cholinergic deficit, but no change in other neurotransmitter systems. Studies in aged rats revealed that treatment with L-Carnitine can restore the level or increase the activity of the neurotransmitter enzyme acetylcholinesterase in the brain<sup>25</sup>. The neuroprotective effects of L-Carnitine are attributed to be either due to unspecific membrane interactions, or, more probable, to its sterical resemblance to the neurotransmitter acetylcholine<sup>26</sup>. Chemically, acetylcholine and L-Carnitine have a very similar structure.

L-Carnitine treatment for 2 months was found to improve the learning ability of old rats and to reduce the loss of cognitive functions that occur with aging<sup>27</sup>. In a labyrinth (T maze) test, L-Carnitine treated animals made significantly less errors. Significantly more animals reached the T-maze goal compared to the same age control group.

A preliminary study with elderly people revealed similar results: supplementation with 4 g L-Carnitine/day resulted in significantly improved mental status compared with the placebo group, assessed by means of the Wesseley and Powell scale<sup>28</sup>.

## L-Carnitine in the muscle

Skeletal muscles contain a high proportion of mitochondria, since they require a lot of energy during work. Thus it is no wonder that they constitute the main reservoir of L-Carnitine in the body and have an L-Carnitine concentration at least 200 times higher than blood plasma. Muscle mass and muscle strength tend to decrease with age<sup>29</sup>. This can lead to a reduction in physical ability and may cause adverse metabolic effects. Analysis of muscle samples of healthy humans of different age showed a drastic reduction of L-Carnitine and acyl-L-Carnitine in the older subjects<sup>30, 31</sup>. Potentially, an alteration of the L-Carnitine carrier in the muscle cell membrane is the reason for muscle L-Carnitine reduction with age<sup>32</sup>.

In healthy adults, Carnipure™ supplementation has been shown to stimulate *in vivo* long chain fatty acid metabolism<sup>33, 34</sup>, which backs up another study: one month's treatment with L-Carnitine in subjects aged from 70 to 92 was found to be associated with a significant increase in total muscle mass, compared with placebo. The total fat mass was reduced at the same time<sup>28</sup>.

## ...and beats and beats and beats

In developed countries, cardiovascular disease is one of the most common causes of death. Chronic diseases or conditions that develop with age all centre around and affect the heart with its vital functions in the body.

In rats, a decrease of L-Carnitine in heart mitochondria with age could be shown<sup>35</sup>. A decrease in myocardial free L-Carnitine has been observed in both experimental animals and humans as a result of acute and chronic myocardial ischaemia<sup>36-38</sup>.

Although L-Carnitine does not affect general or regional hemodynamics, there is evidence that it improves the stress tolerance of the heart by increasing the substrate availability required for energy production<sup>39</sup>. From a review of scientific literature, it is clear that L-Carnitine's benefits are not confined solely to healthy heart function – extensive clinical data indicates that oral L-Carnitine supplementation can be beneficial in helping to maintain normal cholesterol levels in elderly people<sup>28</sup>.

## Immune System

The immune system is a highly complex functional system to fight external substances (antigens) and to eliminate malignant cells of the body. Neutrophils are important cells within the immune system, which respond most rapidly to invasion by pathogens. An age-related decline in neutrophil function may be, in part, responsible for increased morbidity and mortality from infections in the elderly population.

One of the most dramatic and consequence-bearing age-related phenomena is the decline of the immune function with old age<sup>40</sup>, which may predispose to several diseases commonly associated with increasing age<sup>41</sup>.

By stabilizing biomembranes against inflammatory agents, L-Carnitine abolishes the age-related increase in plasma membrane viscosity. It could be shown that L-Carnitine treatment can prevent the decrease in neutrophil chemotactic activity.

Treatment with L-Carnitine was found to prevent the age-related increase of superoxide production by neutrophils in old rats. This effect of L-Carnitine may be related to inhibition of protein kinase C activity. Protein kinase C is an enzyme involved in signalling processes. It is well known that L-Carnitine inhibits the age-related increase in protein kinase C-mediated response in human neutrophils. Overall, although more research is required, L-Carnitine supplementation may be supportive of healthy and general immune function<sup>42</sup>.



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“Some dietary supplements have clear benefits for the elderly in supporting nutritional status, improving immune function, and reducing the risk of some chronic diseases. Those eager for appropriate reform should take care not to turn older citizens away from dietary supplements with proven benefit”, said Dr Annette Dickinson, vice president of the Council for Responsible Nutrition.

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## And so to conclude

With a two-fold increase in the world's elderly predicted between 1998 and 2025, it is not surprising that the market for anti-aging foods and supplements will see increased levels of activity and opportunity for manufacturers. Carnipure™ can be regarded as the ideal nutrient for a long life, as it comprises all the benefits that seniors need to stay fit and healthy in both mind and body.

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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 L-Carnitine 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.

This Carnipure™ Focus has been reviewed by Professor Alfred Lohninger from the University of Vienna, Austria.



## For more information:

Worldwide

**Lonza Ltd, Basel, Switzerland**

Tel +41 61 316 81 11

In the USA

**Lonza Inc, Allendale, NJ**

Tel +1 201 316 9200

[carnipure@lonza.com](mailto:carnipure@lonza.com)

[www.carnipure.com](http://www.carnipure.com)

[www.lonza.com](http://www.lonza.com)



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