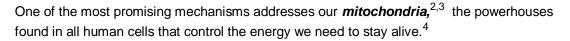
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REPORT

Carnitine Restores Cellular Function

By Logan Bronwell

A wealth of emerging technology demonstrates that as we gain control over individual mechanisms involved in cellular aging, systemic symptoms of **degeneration** can be slowed *or even reversed*.¹





Over time, our mitochondria decrease in both number and function. The result is essentially a short-circuiting of power to every area of your body. Keeping these cellular powerhouses functioning properly can postpone many of the so-called "inevitable" signs of aging. Research now shows that the amino acid **carnitine** can forestall and even reverse many well-known factors of aging.

With advancing age, carnitine levels decline in all of our tissues.^{2,3} That spells trouble for **mitochondria**, which become starved of energy and filled with cellular waste.^{3,4}

Simply put, a *carnitine deficiency* leads to the wholesale destruction of our mitochondria. And, ultimately, this loss of mitochondrial function is likely to hasten death. Fortunately, *carnitine* is sold as a dietary supplement in the United States, available without the need of a doctor's prescription as it is in some other countries.



WHY MITOCHONDRIA DECLINE WITH AGING

Mitochondria reside in *every* cell in our bodies; they power cells by converting food into the energy our body needs to operate.⁴ Think of the mitochondria like the power company that supplies energy to your home. If the power goes out, your food spoils, your heating and air condition won't work, you have no light. The same effect occurs within your body. If the mitochondria—your power supply—isn't functioning properly, or if they decrease in numbers, then your cells won't have the energy they need to power your body's many functions.

As the amount of functioning mitochondria decreases, many of the "symptoms" of aging manifests. In part, this occurs because of the mitochondria's continual burning of fatty acids

to produce energy. In the process of releasing energy, huge bursts of *oxidant* compounds damage **mitochondria** and the cells that contain them.⁴ This steady assault leads to the gradual loss of *mitochondrial function* in all of our tissues.⁵

The age-related decline in *mitochondrial activity* is largely responsible for cardiovascular and neurological disorders as well as obesity and type II diabetes.⁶⁻⁹ Loss of mitochondrial function in muscle tissue also leads to the familiar "flabby" body

composition we associate with older people because it causes muscle atrophy and increased body fat mass.¹⁰ From this list, you can see how essential carnitine is to your daily health.

Total carnitine levels in aging individuals are roughly 20% lower than in youth,¹¹ which leaves mitochondria increasingly vulnerable to damage.

Fortunately, studies have proven that supplementing with carnitine can restore mitochondrial function to near-youthful levels.¹²

CARNITINE REDUCES DEATH RATES

The heart muscle uses fat as its primary energy source. Carnitine is a fat-transporting compound that is absolutely essential for normal heart function.¹³ Over time, the decline of carnitine plays a role in the weakening of the heart's muscles.¹⁴

People with heart muscle damage from heart attacks or heart failure have especially low carnitine levels.¹⁵⁻¹⁷ Fortunately, carnitine supplementation has proven to be remarkably effective in fighting and even reversing the heart-weakening effects from that drop in carnitine levels.¹⁴

In one study, 160 male and female heart attack survivors between 39 and 86 years old received either 4 grams/day of Lcarnitine or a placebo for 12 months.¹⁸ The patients taking L-carnitine experienced significantly favorable decreases in heart rate and blood pressure; they also had improved blood lipid profiles. Most importantly, those supplementing with carnitine had a dramatically reduced death rate compared to those not taking carnitine. Patients taking carnitine had a death rate of just 1.2% in the entire year, while 12.5% of control patients died, with the majority of deaths attributed to repeat heart attacks.¹⁸

L-carnitine supplementation also prevents the progression of heart muscle damage in people with congestive heart failure and improves exercise tolerance in people who develop chest pain (angina) with exertion.¹⁵ In one study, 55% of patients experienced improvement in their standard heart failure classification.¹⁵

People with angina, an early sign of heart muscle threatened by ischemia (low blood flow), benefited from carnitine supplements. A natural derivative of L-carnitine, propionyl-L-carnitine, at a dose of 500 mg 3 times daily, increased the mean time that patients could exercise without EKG signs of ischemia by an impressive 450%.¹⁶ That result indicated improved blood flow to heart muscle cells following ischemia, an effect amply demonstrated in animal studies.^{19,20}

Carnitine also increases concentrations of nitric oxide that help endothelial cells relax and increase blood flow, which can help lower blood pressure.²¹⁻²³ Three weeks of supplementation with **2 grams** of L-carnitine improved blood flow by 17% during the critical after-meal period in a group of people fed a high-fat meal; placebo patients had a 12% decrease in blood flow.²⁴ And a daily 6-gram intravenous dose of propionyl-L-carnitine for one week improved walking distance in people with peripheral arterial disease by 28%.²⁵

TWO GROUPS GAIN EXCEPTIONAL BENEFITS

Two groups stand to gain exceptional benefits from carnitine supplementation: diabetics and those on dialysis. Both groups are at especially high risk for cardiovascular complications and early death, and both groups have an even greater depletion of carnitine than others of the same age.^{17,26}

Dialysis exerts huge stresses on the human body, all of which accelerate atherosclerosis and heart disease. The addition of a 1gram, IV dose of L-carnitine at the end of each dialysis session markedly reduced chemical markers of stress and increased levels of the protective cytokine *adiponectin*.²⁶

The same 1-gram dose, given orally, produced a marked reduction in serum inflammatory markers and factors that promote excessive blood clots.²⁷ Finally, a dose of **10 mg/kg** of carnitine (about **750 mg/day** in an average-sized person) produced a significant **12%** decrease in the size of the heart's left ventricle in dialysis patients.²⁸ That "left ventricular hypertrophy" is a known complication of hemodialysis and contributes to early heart failure.

Diabetics suffer from both *ischemic* (low blood flow) and non-ischemic heart muscle dysfunction, much of which can be reduced by long-term oral L-carnitine supplements.²⁹ Animal studies show that whether you're a diabetic or not, oral

supplementation with L-carnitine helps your heart muscle pump harder and more efficiently.²⁹ Even more impressive, carnitine's mitochondriafriendly actions help reduce body fat mass, which in turn improves insulin sensitivity and may help control blood sugar levels.30,31

WHAT YOU NEED TO KNOW

CARNITINE FIGHTS DIABESITY



As **obesity** rates skyrocket, more and more Americans are developing **type II diabetes** as a result, producing a syndrome called "diabesity."^{32,33}

Since carnitine helps the mitochondria utilize energy, it plays a critical role in reducing the occurrence and impact of diabesity.³⁴ Recent studies show that in addition to helping the mitochondria burn fat as energy, carnitine is also vital for removing waste products from mitochondria.^{2,35} This is important, because we now recognize that the buildup of mitochondrial waste products is one of the most important contributors to insulin resistance, which further promotes high blood sugar and obesity.⁴

ANTI-AGING BENEFITS OF CARNITINE

- A major cause of aging is the decline in function of mitochondria, the tiny powerhouses that energize our cells.
- Most chronic diseases of aging reflect loss of mitochondrial function and numbers, limiting the energy available to cells as we age.
- Poorly-functioning mitochondria also impose huge oxidant stress on their parent cells, further accelerating aging and shortening life.



- L-carnitine, a natural molecule with several related forms, provides mitochondria with both the energy they need and the antioxidant protection that they must have to retain their youthful function.
- Carnitine supplements extend life by increasing energy to tissues throughout the body.
- Carnitine supplementation has proven effective in reducing fatigue, enhancing cardiovascular function, improving body composition and promoting weight loss, lowering blood sugar levels, and delaying or reversing brain degeneration.
- Its energy-releasing properties make carnitine a useful supplement for reducing the deadly cachexia experienced by many cancer patients.

Obesity and aging contribute to low carnitine levels, which compromises mitochondrial

performance and increases insulin resistance, promoting further obesity and carnitine reduction.² Restoring carnitine levels to their youthful values is an effective way to break this deadly cycle.²

Human volunteers who took L-carnitine **3 grams/day** for 10 days had favorable changes in body composition.³⁶ Supplemented patients used their fat for energy, burning it **22%** faster than control patients, without any increase in muscle protein breakdown. Another study, using **2 grams/day** for 6 months, demonstrated a loss of total fat mass of **4 pounds**, with a gain in lean muscle mass of **8.4 pounds**.³⁷

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Animal studies confirm and extend these findings, showing that propionyl-L-carnitine decreases body weight gain, food intake, and fat composition, while improving insulin resistance.³⁴

Carnitine also has multiple favorable effects on blood sugar and insulin resistance, the hallmarks of type II diabetes.³⁵ Animals fed a high fat diet develop the same symptoms and signs that humans do: obesity, insulin resistance, abnormal lipid profiles, and liver damage which are known as **metabolic syndrome**. Just 4 weeks of treatment with L-carnitine reversed all of those abnormal parameters.30,32,38,39

Similar effects have been found in diabetic humans. Two grams of L-carnitine twice daily for 10 days improved insulin sensitivity and reduced insulin levels.⁴⁰ L-carnitine supplementation of **2 grams/day** caused a significant reduction in plasma free fatty acids, which contribute to insulin resistance.⁴¹ Three grams/day were shown to reduce simulated *after-meal* blood sugar spikes from **157 mg/dL** to **132 mg/dL** (oral glucose tolerance test).⁴² A significant number of studies document the deadly impact of elevated *after-meal* glucose levels.

CARNITINE DEFENDS MEMORY

Most forms of age-related memory and cognitive decline are closely related to *mitochondrial dysfunction* in brain tissue. That provides an obvious opportunity for intervention with a mitochondrial enhancer such as carnitine. Most studies of neurodegeneration used the acetyl-Lcarnitine form of carnitine.

The impact of acetyl-L-carnitine is especially important in Alzheimer's disease, the leading cause of dementia and mild cognitive impairment in the United States. One early study showed that supplementing with acetyl-L-carnitine every day for a year led to improvements on the cognitive portion of a standard Alzheimer's disease rating scale in patients younger than 61.⁴³



IMPORTANT FORMS OF CARNITINE

The basic L-carnitine molecule that supports mitochondrial function is available in several forms, each of which offers specific functions:

L-carnitine tartrate is a stable salt form of L-carnitine and has been shown to be absorbed faster than other L-carnitine compounds.⁸¹ It favorably affects biochemical markers of recovery from physical exertion, optimizing the processes of muscle tissue repair and remodeling.⁸²

Acetyl-L-carnitine is a molecule chiefly active in moving fat molecules across the mitochondrial membrane.⁶⁹ It readily crosses into the brain from the bloodstream, and its extra acetyl molecule provides additional energy directly to brain cells.

ArginoCarn®* is a patented form of acetyl-Lcarnitine arginate dihydrochloride that is molecularly bonded to the amino acid arginine and known as the AminoCarnitine® generation. In a way that closely resembles natural nerve growth factor, this compound induces outgrowth of the tiny but essential nerve cell protrusions called neurites that underpin memory formation and learning.⁷⁰

Glycine propionyl-L-carnitine hydrochloride (GlycoCarn®)* is a patented form of AminoCarnitine® that is molecularly bonded to the amino acid glycine and known as the AminoCarnitine® generation. Propionyl-L-carnitine is essential in carbohydrate and lipid metabolism and is a potent antioxidant.³¹ It is especially useful in cardiovascular diseases.³¹ The related glycine form has also been shown to extend those benefits to skeletal muscle, enhancing exercise performance.⁷¹

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More recent studies have shown good effects even in older patients, but, as with all forms of prevention, the earlier you start taking carnitine, the more powerful the effects on memory. Doses

ranging from **1.5** to **3 grams/day** of acetyl-L-carnitine have consistently been shown to produce treatment effects several-fold greater than placebo alone, with the greatest impact in patients in the earlier stages of the disease.⁴⁴⁻⁴⁶ Improvements from

acetyl-L-carnitine supplementation can be seen as early as 3 months, and continue to increase over time.⁴⁵ (Carnitine has not been found effective in patients with advanced Alzheimer's.)

Laboratory studies explain some of the reasons for acetyl-L-carnitine's impact on Alzheimer's disease, and most of them focus on carnitine's mitochondrial protective properties.

Scientists can induce Alzheimer's-like changes in brain cells using a variety of chemical techniques, and they consistently find that treatment with acetyl-l-carnitine enhances mitochondrial function and slows development of those changes, which include accumulation of the "Alzheimer's protein" *amyloid beta* (*Abeta*).⁴⁷ Even after dangerous quantities of *amyloid beta* form in brain tissue, acetyl-L-carnitine treatment reduces its impact.³

Lab animals with conditions similar to Alzheimer's disease demonstrate improved memory and learning when treated with acetyl-

L-carnitine.^{47,48} In fact, treated animals show increased expression of important memory-associated proteins that had become impaired by Alzheimer's disease.⁴⁹

Acetyl-L-carnitine is useful in other forms of cognitive decline as well, even in poorly-defined conditions such as mild cognitive (or mental) impairment. People supplemented with **1.5** to **2 grams** of acetyl-L-carnitine daily show marked improvement on standard mental status and memory scores.^{50,51} These effects are especially impressive among the very old, including at least one study of people over 100 years old.³⁷



CARNITINE BENEFITS BODY COMPOSITION

Carnitine's influence on mitochondrial function can improve age-induced changes in body composition. When lab animals were given carnitine, they experienced reductions in their abdominal fat mass, increases in their muscle strength, and lower concentrations of *leptin*, a cytokine that triggers fat-induced inflammation.^{10,52}

Human volunteers who took **3 grams/day** of L-carnitine for 10 days had favorable changes in body composition.³⁶ Patients taking L-carnitine used their fat for energy, burning it **22%** faster than control patients, and without any increase in muscle protein breakdown. Another study using 2 grams/day demonstrated a loss of total fat mass of **4 pounds**, with a gain in lean muscle mass of **8.4 pounds**.³⁷

Additional studies on animals confirm and extend these findings, showing that propionyl-L-

carnitine decreases body weight gain, food intake, and fat composition, while improving insulin resistance.³⁴

Benefits of supplementation go well beyond memory, however. Not surprisingly for a *mitochondrial function-boosting* compound, improvements in energy level, and reduction in physical and mental fatigue are commonly reported in studies of carnitine supplementation (both with L-carnitine and acetyl-L-carnitine).^{37,53} And a few studies have found improvements in depression while patients supplement with L-carnitine.^{54,55}

Finally, as a result of the obesity epidemic (and with liver disease and cirrhosis on the rise),⁵⁶ researchers are showing a growing interest in using carnitine to optimize liver mitochondrial function and prevent or mitigate the effects of liver failure. Several studies have demonstrated clinical and biochemical improvements in patients with hepatic encephalopathy, a condition in which rising blood ammonia levels impair cognitive and motor function.⁵⁷⁻⁵⁹



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CARNITINE COMBATS CANCER WASTING

One of the most painful and tragic consequences of many cancers is their induction of *cachexia*, the progressive loss of appetite, energy, and body fat, with increased muscle wasting.^{60,61} Cancer cachexia is induced by many factors, the most prominent of which is decreased tissue carnitine levels.⁶⁰⁻⁶² Diminished appetite contributes to poor nutrition and further declines in carnitine levels.^{63,64}

Many strong studies now demonstrate that the carnitine supplements can reduce the rate and severity of cancer cachexia.^{65,66}

Many also show improvements in appetite, fatigue, and quality of life—especially in the form of L-propionyl carnitine.^{61,67,68}

EXERCISE-RELATED BENEFITS OF CARNITINE

- Carnitine reduces exercise-induced oxidative stress. Studies show that carnitine sharply reduces harmful fat
 oxidation byproducts in muscle tissue.⁷²⁻⁷⁷
- Carnitine reduces fatigue following moderate exercise. A study of middle-aged men and women showed that 2 grams/day of L-carnitine improved recovery time after physical exertion.⁷⁸ A human study done with kidney patients on hemodialysis (a group chronically plagued by fatigue) showed that a large IV dose of carnitine could increase the amount of time they were able to exercise before becoming fatigued by 22%—while also beneficially lowering heart rates.⁷⁶
- Carnitine enhances muscle performance and endurance.^{10,72,79} One study in animals demonstrated a **39%** increase in the distance the animals were able to run before they experienced exhaustion in normal air, and an astonishing **50%** increase when the animals ran under low-oxygen conditions.⁷⁹
- Carnitine increases exercise tolerance for people who experience angina with exertion.³⁰ Patients taking **500 mg** 3 times daily of propionyl-L-carnitine (a natural derivative of L-carnitine) experienced a **450%** increase in the mean time they could exercise without EKG signs of ischemia.³¹ That result indicated improved blood flow to heart muscle cells following ischemia, an effect proven time and again in animal studies.^{34,35}
- Carnitine enhances the performance of trained endurance athletes. One study showed that 2 grams/day of L-carnitine reduced heart rates and lowered blood sugar levels during exercise.⁸⁰ Another study demonstrated that athletes using 4.5 grams/day of glycine propionyl-L-carnitine experienced increased muscle power with decreased fatigue-inducing lactic acid accumulation.⁷¹

SUMMARY

Loss of mitochondrial function is a major contributor to the process of aging. It deprives vital tissues in our body of the energy they need to perform normal tasks and to keep us vibrant, healthy, and young. Carnitine, a natural facilitator of energy transport in mitochondria, is essential for keeping mitochondria healthy and preventing their age-related loss.

Supplementing with carnitine can help preserve cell energy levels, reduce fatigue, enhance heart muscle strength, reduce the impact of obesity and diabetes, slow signs of brain aging, and protect heart attack victims from dying.

If you have any questions on the scientific content of this article, please call a Life Extension® Health Advisor at 1-866-864-3027.

REFERENCES

- 1. Ames BN. Optimal micronutrients delay mitochondrial decay and age-associated diseases. *Mech Ageing Dev.* 2010 JulAug;131(7-8):473-9.
- 2. Noland RC, Koves TR, Seiler SE, et al. Carnitine insufficiency caused by aging and overnutrition compromises mitochondrial performance and metabolic control. *J Biol Chem.* 2009 Aug 21;284(34):22840-52.
- 3. Abdul HM, Calabrese V, Calvani M, Butterfield DA. Acetyl-L-carnitine-induced up-regulation of heat shock proteins protects cortical neurons against amyloid-beta peptide 1-42-mediated oxidative stress and neurotoxicity: implications for Alzheimer's disease. *J Neurosci Res.* 2006 Aug 1;84(2):398-408.
- 4. Terman A, Kurz T, Navratil M, Arriaga EA, Brunk UT. Mitochondrial turnover and aging of long-lived postmitotic cells: the mitochondrial-lysosomal axis theory of aging. *Antioxid Redox Signal.* 2010 Apr;12(4):503-35.
- 5. Parise G, De Lisio M. Mitochondrial theory of aging in human age-related sarcopenia. *Interdiscip Top Gerontol.* 2010;37:142-56.
- 6. Chakrabarti S, Munshi S, Banerjee K, Thakurta IG, Sinha M, Bagh MB. Mitochondrial dysfunction during brain aging: role of oxidative stress and modulation by antioxidant supplementation. *Aging Dis.* 2011 Jun;2(3):242-56.
- 7. Dutta D, Calvani R, Bernabei R, Leeuwenburgh C, Marzetti E. Contribution of impaired mitochondrial autophagy to cardiac aging: mechanisms and therapeutic opportunities. *Circ Res.* 2012 Apr 13;110(8):1125-38.
- 8. Maasen JA. Mitochondria, body fat and type 2 diabetes: what is the connection? *Minerva Med.* 2008 Jun;99(3):241-51.
- 9. Wang CH, Wang CC, Wei YH. Mitochondrial dysfunction in insulin insensitivity: implication of mitochondrial role in type 2 diabetes. *Ann N Y Acad Sci.* 2010 Jul;1201:157-65.
- Bernard A, Rigault C, Mazue F, Le Borgne F, Demarquoy J. L-carnitine supplementation and physical exercise restore age-associated decline in some mitochondrial functions in the rat. *J Gerontol A Biol Sci Med Sci.* 2008 Oct;63(10):102733.
- 11. Tanaka Y, Sasaki R, Fukui F, et al. Acetyl-L-carnitine supplementation restores decreased tissue carnitine levels and impaired lipid metabolism in aged rats. *J Lipid Res.* 2004 Apr;45(4):729-35.
- Pesce V, Fracasso F, Cassano P, Lezza AM, Cantatore P, Gadaleta MN. Acetyl-L-carnitine supplementation to old rats partially reverts the age-related mitochondrial decay of soleus muscle by activating peroxisome proliferator-activated receptor gamma coactivator-1alpha-dependent mitochondrial biogenesis. *Rejuvenation Res.* 2010 Apr-Jun;13(2-3):148-51.
- Chao HH, Chen CH, Liu JC, Lin JW, Wong KL, Cheng TH. L-Carnitine attenuates angiotensin II-induced proliferation of cardiac fibroblasts: role of NADPH oxidase inhibition and decreased sphingosine-1-phosphate generation. *J Nutr Biochem.* 2010 Jul;21(7):580-8.
- 14. Gomez LA, Heath SH, Hagen TM. Acetyl-L-carnitine supplementation reverses the age-related decline in carnitine palmitoyltransferase 1 (CPT1) activity in interfibrillar mitochondria without changing the L-carnitine content in the rat heart. *Mech Ageing Dev.* 2012 Feb-Mar;133(2-3):99-106.
- 15. Kobayashi A, Masumura Y, Yamazaki N. L-carnitine treatment for congestive heart failure--experimental and clinical study. *Jpn Circ J.* 1992 Jan;56(1):86-94.
- 16. Bartels GL, Remme WJ, den Hartog FR, Wielenga RP, Kruijssen DA. Additional antiischemic effects of long-term Lpropionylcarnitine in anginal patients treated with conventional antianginal therapy. *Cardiovasc Drugs Ther.* 1995 Dec;9 (6):749-53.
- 17. Molyneux R, Seymour AM, Bhandari S. Value of carnitine therapy in kidney dialysis patients and effects on cardiac function from human and animal studies. *Curr Drug Targets.* 2012 Feb;13(2):285-93.
- 18. Davini P, Bigalli A, Lamanna F, Boem A. Controlled study on L-carnitine therapeutic efficacy in post-infarction. *Drugs Exp Clin Res.* 1992;18(8):355-65.
- 19. Stasi MA, Scioli MG, Arcuri G, et al. Propionyl-L-carnitine improves postischemic blood flow recovery and arteriogenetic revascularization and reduces endothelial NADPH-oxidase 4-mediated superoxide production. *Arterioscler Thromb Vasc Biol.* 2010 Mar;30(3):426-35.
- 20. Lapi D, Sabatino L, Altobelli GG, Mondola P, Cimini V, Colantuoni A. Effects of propionyl-L-carnitine on ischemiareperfusion injury in hamster cheek pouch microcirculation. *Front Physiol.* 2010;1:132.
- 21. Gomez-Amores L, Mate A, Miguel-Carrasco JL, et al. L-carnitine attenuates oxidative stress in hypertensive rats. *J Nutr Biochem.* 2007 Aug;18(8):533-40.
- 22. Alvarez de Sotomayor M, Bueno R, Perez-Guerrero C, Herrera MD. Effect of L-carnitine and propionyl-L-carnitine on endothelial function of small mesenteric arteries from SHR. *J Vasc Res.* 2007;44(5):354-64.
- 23. de Sotomayor MA, Mingorance C, Rodriguez-Rodriguez R, Marhuenda E, Herrera MD. I-carnitine and its propionate: improvement of endothelial function in SHR through superoxide dismutase-dependent mechanisms. *Free Radic Res.* 2007 Aug;41(8):884-91.
- 24. Volek JS, Judelson DA, Silvestre R, et al. Effects of carnitine supplementation on flow-mediated dilation and vascular inflammatory responses to a high-fat meal in healthy young adults. *Am J Cardiol.* 2008 Nov 15;102(10):1413-7.
- 25. Loffredo L, Pignatelli P, Cangemi R, et al. Imbalance between nitric oxide generation and oxidative stress in patients with peripheral arterial disease: effect of an antioxidant treatment. *J Vasc Surg.* 2006 Sep;44(3):525-30.

- 26. Csiky B, Nyul Z, Toth G, et al. L-carnitine supplementation and adipokines in patients with end-stage renal disease on regular hemodialysis. *Exp Clin Endocrinol Diabetes*. 2010 Nov;118(10):735-40.
- 27. Hakeshzadeh F, Tabibi H, Ahmadinejad M, Malakoutian T, Hedayati M. Effects of L-Carnitine supplement on plasma coagulation and anticoagulation factors in hemodialysis patients. *Ren Fail.* 2010;32(9):1109-14.
- 28. Sakurabayashi T, Miyazaki S, Yuasa Y, et al. L-carnitine supplementation decreases the left ventricular mass in patients undergoing hemodialysis. *Circ J.* 2008 Jun;72(6):926-31.
- 29. Keller VA, Toporoff B, Raziano RM, Pigott JD, Mills NL. Carnitine supplementation improves myocardial function in hearts from ischemic diabetic and euglycemic rats. *Ann Thorac Surg.* 1998 Nov;66(5):1600-3.
- 30. Mingorance C, Duluc L, Chalopin M, et al. Propionyl-L-carnitine corrects metabolic and cardiovascular alterations in dietinduced obese mice and improves liver respiratory chain activity. *PLoS One.* 2012;7(3):e34268.
- 31. Mingorance C, Rodriguez-Rodriguez R, Justo ML, Herrera MD, de Sotomayor MA. Pharmacological effects and clinical applications of propionyl-L-carnitine. *Nutr Rev.* 2011 May;69(5):279-90.
- 32. Amin KA, Nagy MA. Effect of Carnitine and herbal mixture extract on obesity induced by high fat diet in rats. *Diabetol Metab Syndr.* 2009;1(1):17.
- 33. Mangou A, Grammatikopoulou MG, Mirkopoulou D, Sailer N, Kotzamanidis C, Tsigga M. Associations between diet quality, health status and diabetic complications in patients with type 2 diabetes and comorbid obesity. *Endocrinol Nutr.* 2012 Feb;59(2):109-16.
- 34. Mingorance C, Gonzalez del Pozo M, Dolores Herrera M, Alvarez de Sotomayor M. Oral supplementation of propionyl-Icarnitine reduces body weight and hyperinsulinaemia in obese Zucker rats. *Br J Nutr.* 2009 Oct;102(8):1145-53.
- Ringseis R, Keller J, Eder K. Role of carnitine in the regulation of glucose homeostasis and insulin sensitivity: evidence from in vivo and in vitro studies with carnitine supplementation and carnitine deficiency. *Eur J Nutr.* 2012 Feb;51(1):1-18.
- 36. Wutzke KD, Lorenz H. The effect of I-carnitine on fat oxidation, protein turnover, and body composition in slightly overweight subjects. *Metabolism.* 2004 Aug;53(8):1002-6.
- 37. Malaguarnera M, Cammalleri L, Gargante MP, Vacante M, Colonna V, Motta M. L-Carnitine treatment reduces severity of physical and mental fatigue and increases cognitive functions in centenarians: a randomized and controlled clinical trial. *Am J Clin Nutr.* 2007 Dec;86(6):1738-44.
- Kang JS, Lee WK, Yoon WK, et al. A combination of grape extract, green tea extract and L-carnitine improves high-fat diet-induced obesity, hyperlipidemia and non-alcoholic fatty liver disease in mice. *Phytother Res.* 2011 Dec;25(12):178995.
- 39. Xia Y, Li Q, Zhong W, Dong J, Wang Z, Wang C. L-carnitine ameliorated fatty liver in high-calorie diet/STZ-induced type 2 diabetic mice by improving mitochondrial function. *Diabetol Metab Syndr.* 2011;3:31.
- Molfino A, Cascino A, Conte C, Ramaccini C, Rossi Fanelli F, Laviano A. Caloric restriction and L-carnitine administration improves insulin sensitivity in patients with impaired glucose metabolism. *JPEN J Parenter Enteral Nutr.* 2010 May-Jun;34 (3):295-9.
- 41. Lohninger A, Radler U, Jinniate S, et al. Relationship between carnitine, fatty acids and insulin resistance. *Gynakol Geburtshilfliche Rundsch.* 2009;49(4):230-5.
- 42. Galloway SD, Craig TP, Cleland SJ. Effects of oral L-carnitine supplementation on insulin sensitivity indices in response to glucose feeding in lean and overweight/obese males. *Amino Acids.* 2011 Jul;41(2):507-15.
- 43. Brooks JO, 3rd, Yesavage JA, Carta A, Bravi D. Acetyl L-carnitine slows decline in younger patients with Alzheimer's disease: a reanalysis of a double-blind, placebo-controlled study using the trilinear approach. *Int Psychogeriatr.* 1998 Jun;10(2):193-203.
- 44. Gavrilova SI, Kalyn Ia B, Kolykhalov IV, Roshchina IF, Selezneva ND. Acetyl-L-carnitine (carnicetine) in the treatment of early stages of Alzheimer's disease and vascular dementia. *Zh Nevrol Psikhiatr Im S S Korsakova*. 2011;111(9):16-22.
- 45. Montgomery SA, Thal LJ, Amrein R. Meta-analysis of double blind randomized controlled clinical trials of acetyl-Lcarnitine versus placebo in the treatment of mild cognitive impairment and mild Alzheimer's disease. *Int Clin Psychopharmacol.* 2003 Mar;18(2):61-71.
- 46. Bianchetti A, Rozzini R, Trabucchi M. Effects of acetyl-L-carnitine in Alzheimer's disease patients unresponsive to acetylcholinesterase inhibitors. *Curr Med Res Opin.* 2003;19(4):350-3.
- 47. Zhou P, Chen Z, Zhao N, et al. Acetyl-L-carnitine attenuates homocysteine-induced Alzheimer-like histopathological and behavioral abnormalities. *Rejuvenation Res.* 2011 Dec;14(6):669-79.
- 48. Yin YY, Liu H, Cong XB, et al. Acetyl-L-carnitine attenuates okadaic acid induced tau hyperphosphorylation and spatial memory impairment in rats. *J Alzheimers Dis.* 2010;19(2):735-46.
- 49. Jiang X, Tian Q, Wang Y, et al. Acetyl-L-carnitine ameliorates spatial memory deficits induced by inhibition of phosphoinositol-3 kinase and protein kinase C. *J Neurochem.* 2011 Sep;118(5):864-78.
- 50. Salvioli G, Neri M. L-acetylcarnitine treatment of mental decline in the elderly. *Drugs Exp Clin Res.* 1994;20(4):169-76.
- 51. Ames BN, Liu J. Delaying the mitochondrial decay of aging with acetylcarnitine. *Ann N Y Acad Sci.* 2004 Nov;1033:10816.

52. Cha YS. Effects of L-carnitine on obesity, diabetes, and as an ergogenic aid. *Asia Pac J Clin Nutr.* 2008;17 Suppl 1:306-

8.

- 53. Malaguarnera M, Gargante MP, Cristaldi E, et al. Acetyl L-carnitine (ALC) treatment in elderly patients with fatigue. *Arch Gerontol Geriatr.* 2008 Mar-Apr;46(2):181-90.
- 54. Soczynska JK, Kennedy SH, Chow CS, Woldeyohannes HO, Konarski JZ, McIntyre RS. Acetyl-L-carnitine and alphalipoic acid: possible neurotherapeutic agents for mood disorders? *Expert Opin Investig Drugs.* 2008 Jun;17(6):827-43.
- 55. Geier DA, Kern JK, Davis G, et al. A prospective double-blind, randomized clinical trial of levocarnitine to treat autism spectrum disorders. *Med Sci Monit.* 2011 Jun;17(6):PI15-23.
- 56. Tuyama AC, Chang CY. Non alcoholic fatty liver disease. *J Diabetes*. 2012 May 4.
- 57. Malaguarnera M, Vacante M, Giordano M, et al. Oral acetyl-L-carnitine therapy reduces fatigue in overt hepatic encephalopathy: a randomized, double-blind, placebo-controlled study. *Am J Clin Nutr.* 2011 Apr;93(4):799-808.
- 58. Malaguarnera M, Vacante M, Motta M, et al. Acetyl-L-carnitine improves cognitive functions in severe hepatic encephalopathy: a randomized and controlled clinical trial. *Metab Brain Dis.* 2011 Dec;26(4):281-9.
- 59. Malaguarnera M, Bella R, Vacante M, et al. Acetyl-L-carnitine reduces depression and improves quality of life in patients with minimal hepatic encephalopathy. *Scand J Gastroenterol.* 2011 Jun;46(6):750-9.
- 60. Vinci E, Rampello E, Zanoli L, Oreste G, Pistone G, Malaguarnera M. Serum carnitine levels in patients with tumoral cachexia. *Eur J Intern Med.* 2005 Oct;16(6):419-23.
- 61. Silverio R, Laviano A, Rossi Fanelli F, Seelaender M. I-carnitine and cancer cachexia: Clinical and experimental aspects. *J Cachexia Sarcopenia Muscle.* 2011 Mar;2(1):37-44.
- 62. Szefel J, Kruszewski WJ, Ciesielski M, et al. L-carnitine and cancer cachexia. I. L-carnitine distribution and metabolic disorders in cancer cachexia. *Oncol Rep.* 2012 Jul;28(1):319-23.
- 63. Malaguarnera M, Risino C, Gargante MP, et al. Decrease of serum carnitine levels in patients with or without gastrointestinal cancer cachexia. *World J Gastroenterol.* 2006 Jul 28;12(28):4541-5.
- 64. Szefel J, Kruszewski WJ, Ciesielski M, et al. L-carnitine and cancer cachexia. II. Effects of lipid emulsion used in total parenteral nutrition on parameters of hemostasis and inflammatory state in L-carnitine deficiency in myocytes. *Oncol Rep.* 2012 Jul;28(1):324-9.
- 65. Liu S, Wu HJ, Zhang ZQ, et al. L-carnitine ameliorates cancer cachexia in mice by regulating the expression and activity of carnitine palmityl transferase. *Cancer Biol Ther.* 2011 Jul 15;12(2):125-30.
- 66. Busquets S, Serpe R, Toledo M, et al. I-Carnitine: An adequate supplement for a multi-targeted anti-wasting therapy in cancer. *Clin Nutr.* 2012 May 18.
- 67. Maccio A, Madeddu C, Gramignano G, et al. A randomized phase III clinical trial of a combined treatment for cachexia in patients with gynecological cancers: evaluating the impact on metabolic and inflammatory profiles and quality of life. *Gynecol Oncol.* 2012 Mar;124(3):417-25.
- 68. Laviano A, Molfino A, Seelaender M, et al. Carnitine administration reduces cytokine levels, improves food intake, and ameliorates body composition in tumor-bearing rats. *Cancer Invest.* 2011 Dec;29(10):696-700.
- 69. Scafidi S, Fiskum G, Lindauer SL, et al. Metabolism of acetyl-L-carnitine for energy and neurotransmitter synthesis in the immature rat brain. *J Neurochem.* 2010 Aug;114(3):820-31.
- 70. Taglialatela G, Navarra D, Olivi A, et al. Neurite outgrowth in PC12 cells stimulated by acetyl-L-carnitine arginine amide. *Neurochem Res.* 1995 Jan;20(1):1-9.
- 71. Jacobs PL, Goldstein ER, Blackburn W, Orem I, Hughes JJ. Glycine propionyl-L-carnitine produces enhanced anaerobic work capacity with reduced lactate accumulation in resistance trained males. *J Int Soc Sports Nutr.* 2009;6:9.
- 72. Brass EP, Adler S, Sietsema KE, Hiatt WR, Orlando AM, Amato A. Intravenous L-carnitine increases plasma carnitine, reduces fatigue, and may preserve exercise capacity in hemodialysis patients. *Am J Kidney Dis.* 2001 May;37(5):101828.
- 73. Sachan DS, Hongu N, Johnsen M. Decreasing oxidative stress with choline and carnitine in women. *J Am Coll Nutr.* 2005 Jun;24(3):172-6.
- 74. Dutta A, Ray K, Singh VK, Vats P, Singh SN, Singh SB. L-carnitine supplementation attenuates intermittent hypoxiainduced oxidative stress and delays muscle fatigue in rats. *Exp Physiol.* 2008 Oct;93(10):1139-46.
- 75. Bloomer RJ, Smith WA. Oxidative stress in response to aerobic and anaerobic power testing: influence of exercise training and carnitine supplementation. *Res Sports Med.* 2009 Jan-Mar;17(1):1-16.
- 76. Fatouros IG, Douroudos I, Panagoutsos S, et al. Effects of L-carnitine on oxidative stress responses in patients with renal disease. *Med Sci Sports Exerc.* 2010 Oct;42(10):1809-18.
- 77. Siktar E, Ekinci D, Beydemir S, Gulcin I, Gunay M. Protective role of L-carnitine supplementation against exhaustive exercise induced oxidative stress in rats. *Eur J Pharmacol.* 2011 Oct 15;668(3):407-13.
- 78. Ho JY, Kraemer WJ, Volek JS, et al. I-Carnitine I-tartrate supplementation favorably affects biochemical markers of recovery from physical exertion in middle-aged men and women. *Metabolism.* 2010 Aug;59(8):1190-9.
- 79. Panjwani U, Thakur L, Anand JP, et al. Effect of L-carnitine supplementation on endurance exercise in normobaric/normoxic and hypobaric/hypoxic conditions. *Wilderness Environ Med.* 2007 Fall;18(3):169-76.

- Broad EM, Maughan RJ, Galloway SD. Effects of exercise intensity and altered substrate availability on cardiovascular and metabolic responses to exercise after oral carnitine supplementation in athletes. *Int J Sport Nutr Exerc Metab.* 2011 Oct;21(5):385-97.
- 81. Eder K, Felgner J, Becker K, Kluge H. Free and total carnitine concentrations in pig plasma after oral ingestion of various Lcarnitine compounds. Int J Vitam Nutr Res. 2005 Jan;75(1):3-9.
- 82. Ho JY, Kraemer WJ, Volek JS, et al. I-Carnitine I-tartrate supplementation favorably affects biochemical markers of recovery from physical exertion in middle-aged men and women. Metabolism. 2010 Aug;59(8):1190-9.

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