Technical Bulletin

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The information in this article is not intended as medical advise, but only as a guide in working with your health care professional.
The information in this bulletin has not been evaluated by the Food & Drug Administration.

"The Metabolic Advantage" Staying Young with SignaCell AM™

Anti-aging scientists are speculating that it is quite possible for humans to achieve a 120 year life span.

This immediately raises two questions:

1. **Why, then, do so few of us reach this potential?**
2. **Is it desirable to live to 120 years?**

Most would agree that living over a century is an advantage if we could avoid the diseases that seem to accompany aging, including pain and suffering, age related macular degeneration (ARMD), age associated mitochondrial decay (AAMD), declining cellular energy (DCE), free radical damage and advanced glycation end products (AGE).

New Spirit Naturals is excited to be working with some extraordinary products that have the strong potential for influencing these metabolic processes to keep us younger, longer.

It has been said that there is a finite amount of energy available in the Universe that can be converted to different forms, but never created or destroyed according to the law of thermodynamics. On earth, energy flows from the sun to produce fuel to support our existence. Plants convert radiant energy from the sun into energy during a process called photosynthesis. Animals and humans draw on this power by eating plants or by eating other animals that have consumed these energy-laden plants.

In our body, foods must be broken down into simpler compounds that are available to the cells. Cells, in turn, manufacture chemical energy, allowing the body to exert physical energy. The science of how the body extracts and uses energy from food is referred to as *energy metabolism* or *bioenergetics*.

Step 1
Carbohydrates are converted to glucose (sugar), fats are converted to glycerol (a triglyceride) and fatty acids and protein are broken down into amino acids. The body then oxidizes these food substances to create energy-rich nutrients.

Step 2
Once these nutrients are delivered to the cells, they are chemically transformed in the mitochondria to the energy molecule adenosine triphosphate (ATP) through a metabolic process known as the Kreb's Cycle. By breaking down into still simpler substances, ATP releases the energy necessary to drive body functions such as respiration and heart beat and fuel the many physical tasks the body is called on to perform.

The complex task of producing ATP cannot occur without protein • enzymes • vitamins • minerals.

Without these, we simply run out of energy, hence the importance of a good supplement program.

- Food based enzymes insure digestion, allowing our metabolic enzymes to function more efficiently.
- Antioxidants are essential for the body to combat free radicals that often wreak havoc on healthy energy producing cells, causing them to struggle to maintain their normal function.
- Minerals supply the electrical spark of life.

Age Associated Mitochondrial Decay (AAMD)

Mitochondria are tiny structures within the cells that convert nutrients into energy through a process called *cellular respiration*. It has been proposed that mitochondrial decay, which results in a decline in cellular energy production, may be one of the most important causes of cellular decline or aging. (Jorday, 1999)
Evidence strongly indicates that ***AAMD is the result of a lack of micronutrients in the cells, compounded by free radical damage***. Our modern medical system, while providing revolutionary treatment of many disorders, often opts for crisis management to address the symptoms of disease, overlooking the fact that many diseases are the final manifestation of a lengthy and silent biochemical and cellular breakdown.

Metabolic Advantage: SignaCell AM™

Just as disease begins at the metabolic level, so, too, does health. New Spirit Naturals' ***Metabolic Advantage Program*** is based on the assumption that a proper combination of nutrients can provide metabolic support to remove or minimize the cause of cellular damage, which, if not addressed, can ultimately evolve into a significant deficiency in energy, accelerated aging and advanced disease. Such compounds include multiple vitamins and minerals, *Acetyl-L-carnitine, Coenzyme Q10, Omega III fatty acids, enzymes and ORAC tested antioxidants.*

Acetyl-L-carnitine
L-carnitine is a naturally occurring compound found primarily in meat and animal products. The body can make approximately 40% of its carnitine requirements through endogenous synthesis in the liver and kidneys. To do so, it needs L-lysine and L-methionine plus other cofactors including niacin, B_6, B_{12}, vitamin C, folic acid and iron plus several enzymes. A shortage of any of these elements can lower the body's level of carnitine.

L-Carnitine Metabolic Actions
L-carnitine plays a key role in many bioenergetic processes. Its availability is an important factor controlling not only the utilization of fatty acids and ketone bodies, but also that of glucose and some amino acids.

Its primary role is the transport of fatty acids into the mitochondria for the production of energy.
L-carnitine is the only carrier used by long chain fatty acids to cross from the cytoplasm through the inner mitochondrial membrane where they undergo B-oxidation and consequent energy production.

It modulates the acetyl-CoA/free CoA ratio in the mitochondria
The enzyme carnitine acetyltransferase (CAT) catalyzes the reaction between L-carnitine and acetyl-CoA, increasing the amount of free coenzyme A which is essential for lipid and carbohydrate utilization. The acetyl groups that result from this reaction are transported out of the mitochondria and are, thereby, available for other cell functions such as acetylcholine synthesis.

L-carnitine also enhances the metabolic flux in the Krebs Cycle and prevents the accumulation of long chain acyl-CoA (LC-acyl-CoA) The importance of L-carnitine in modulating the acyl CoA/CoA ratio is shown by the biochemical changes that occur in metabolically compromised tissue, such as anoxic and ischemic tissue.

It eliminates selective acyl residues, an important detoxification function.
L-carnitine also shuttles acyl moieties from peroxisomes to mitochondria for further oxidation. This is the so called "obligatory" role for L-carnitine because it shuttles activated acyl units from one metabolic component to another for further metabolism.

It is a reservoir of activated acetyl units
Each heart cells contains over 5,000 mitochondria, an indication of its intense need for energy. The heart utilizes fatty acids as a main substrate for the production of energy. The rate of fatty acid uptake by the cardiac muscles is controlled by 1) the availability of exogenous fatty acids; 2) the rate of acyl translocation across the mitochondrial membrane, and 3) the rate of acetyl CoA oxidation by the Krebs Cycle.

It acts as an ATP independent reservoir.
Activated acyl groups are involved in the re-acylation of membrane phospholipids during acute periods of energy depletion.

Nutritional Uses of L-carnitine

Supplementing the diet with L-carnitine is important for people that want to keep fit and maintain a feeling of general well-being and vitality.

Sports Nutrition

Even marginal deficiencies of essential nutrients like carnitine can reduce endurance, prolong recovery time or make it more difficult to improve performance. The majority of carnitine in the body is found in the skeletal muscles. An increase in metabolism, such as during prolonged exercise, reduces the physiological concentration of free carnitine in the muscle. Supplementing with carnitine can moderately increase this concentration, effecting the regulation of carbohydrate metabolism and preventing the accumulation of lactic acid in the blood and tissues. The result is a faster recovery to the resting value lactate/pyruvate ratio.

Weight management and Energy Enhancement

Without L-carnitine, it would be impossible to burn the amount of fat necessary to produce the energy we need to survive. L-carnitine transports fatty acids into the mitochondria, regulating the amount of fat the body can burn, just like a carburetor regulates the amount of gasoline a car can burn. Because of its role as a regulator in the fat-burning process, it follows that it plays an important role in regulating weight and increasing energy levels.

Infant Nutrition

When healthy babies are breast fed, there is little need for supplemental L-carnitine which is well supplied by mother's milk. Babies that are fed soy based formulas or cow's milk formulas may need supplementation. Soy does not contain L-carnitine. Cows milk contains some L-carnitine, but some of this important nutrient is lost during pasteurization. Pre-term babies have a very low capacity for L-carnitine synthesis and storage, but a very high need for L-carnitine. L-carnitine supplementation is, therefore, necessary to improve their growth and development

Note: Both the US and EU indicate the amount of L-carnitine that must be present in infant formulas.

Children's Nutrition

Because children are in the most important stage of growth, they have special dietary needs. Daily supplementation with L-carnitine helps enhance physical growth and mental performance. (Biosent, 2002)

During demanding activities such as play, study and sports, L-carnitine is especially crucial to improve learning, memory, mental sharpness and endurance.

Aging

Tissue levels of L-carnitine decrease progressively as we age. This makes L-carnitine supplementation especially important for older adults. The heart and skeletal muscles are particularly prone to significant L-carnitine deficiency.

L-carnitine supplementation provides older adults with significant beneficial effects, including:

- Improved physical performance
- Improved lipid metabolism
- Enhanced detoxification
- Improved heart and lung function
- Improved immune function
- Improved neuro-protection

Cardiovascular Health

L-carnitine is a key nutrient for cardiac tissue and has been shown to have clinical benefits. In reduced oxygen conditions, like myocardial ischemia, there is an increase of long chain acyl derivatives. These derivatives damage cell and mitochondrial membranes and inhibit energy production. L-carnitine is the only compound that disperses long-chain acyl derivatives. As such, it improves energy metabolism and maintains cell structure.

As an additional benefit, L-carnitine has been shown to modulate lipid composition by elevating high density lipoproteins (HDL) and reducing serum lipid levels (e.g. lipoprotein). Both are factors which are critical in the prevention of atherosclerosis and heart disease.

Pet Food and Animal Food

Studies have shown that L-carnitine is an important nutrient for promoting the performance and well-being of both domestic and farm animals. Since animals have metabolic pathways similar to those found in man, they are subject to many of the same nutritional deficiencies, metabolic disturbances and stress responses.

Additional benefits of Supplementing with Acetyl-L-carnitine

- It plays multiple roles in cellular functions
- It affects cellular metabolism, especially in nerve cells and the highly differentiated cells such as sperm cells.
- It is involved in the biosynthesis of the neurotransmitter acetylcholine which is vital to brain function.
- It readily crosses the blood-brain barrier and increases the activity of the enzyme which produces acetylcholine.
- It is a mitochondriotropic substance necessary for optimal mitochondrial function.
- It makes neurons a preferred target for the metabolic actions of ALC.
- It displays cholinomimetic activity.
- It has a beneficial effect in various neuro-degenerative diseases associated with aging, such as memory and cognitive loss.
- It helps prevent reactive oxygen species (ROS) damage to the inner mitochondrial membrane, preventing its destabilization.
- It improves metabolic potential
- It exerts a neuro-protective action on various conditions of metabolic stress, including ischemia, hypoxia, aging, alcohol abuse and diabetes.
- It can improve memory, learning and mood levels.
- It has multiple neuromodulatory and neurotropic properties.
- It improves symptoms of depression as well as cognitive parameters in aging, Alzheimers disease and chronic alcoholism.

Deficiency or low levels of L-carnitine can be caused by:

- A vegetarian diet. The L-carnitine concentration in vegetables and fruits is less than 1% that of meats. Cereal products contain only 5% of the carnitine of meats.
- Lack of L-carnitine precursors, primarily methionine, lysine, iron, vitamin C, pyridoxine and niacin.
- Genetic defects in L-carnitine biosynthesis.
- Defective intestinal absorption of L-carnitine.
- Increased L-carnitine requirements because of a high fat diet or drugs (e.g. valproic acid, metabolic stress or disease.)

Potential uses of Carnitine

- Prevention of negative age-related changes in the mitochondria and cellular metabolism.
- Prevention of protein damage in diabetes.
- Enhancement of athletic performance
- Protection against:

Dietary deficiencies from vegitarian diets	Free radical damage
Type II Diabetes	Heart Disease
Chronic Fatigue syndrome	Peripheral artery disease
Geriatric depression	Fragile X Syndrome
Alzheimers Disease, particularly in the early stages	HIV
Cognitive defects associated with alcoholism	Neuropathies (drug-induced, diabetic, idiopathic)

Alpha Lipoic Acid - the “Universal Antioxidant”

Unstable molecules known as free radicals are widely recognized for their role in accelerating the aging process and contributing to serious health problems. These free radicals are generated by pollution in our environment and are a by-product of our own hot burning metabolism. The body has a protective antioxidant system to guard against damage that is inflicted by free radicals. In addition, nutrients called antioxidants are essential in boosting the body’s protection against these very active molecules. **Alpha Lipoic Acid** is a key antioxidant that is manufactured in small quantities by the body. It is also found in our foods.

In addition to having antioxidant properties, Alpha Lipoic Acid promotes cellular and muscular energy and functions as a coenzyme in the metabolism of sugars. It is necessary whenever increased energy or strenuous physical activity is required.

It also serves as a cofactor for some of the key enzymes (alpha keto acid dehydrogenases) involved in generating energy from food and oxygen in the mitochondria.

Alpha Lipoic Acid helps supply energy to the brain and has been said to boost the effectiveness of the immune system. In Europe, Alpha Lipoic Acid has been promoted for its ability to help maintain and restore liver health.

One of the most beneficial effects of Alpha Lipoic Acid and DHLA (its reduced form) is their ability to regenerate other essential antioxidants such as vitamin C, vitamin E, coenzyme Q_{10} and glutathione.

Currently, there are both animal and human studies that confirm the use of Alpha Lipoic Acid to prevent and treat diabetes, both Type I and Type II (Adult Onset Diabetes) and their complications. Among the most severe complications of diabetes is nerve damage, especially in the eye (retinopathy) and heart attacks resulting from atherosclerosis. The two most popular mechanisms of action proposed as the cause of these consequences of diabetes are excessive free radical damage and glycosylation (or glycation), where protein molecules bind to glucose molecules in the body to form cross-linked structures. Glycosylation is most evident in senile dementia, stiffening of the arterial system and degenerative diseases of the eyes.

Animal Studies have also shown that Alpha Lipoic Acid can improve glucose utilization in skeletal muscle, the heart muscle and other tissues. One study using Zucker rats as an animal model of obese rats prone to Type II diabetes demonstrated that Alpha Lipoic Acid treatment markedly increased the utilization of glucose in both the absence or presence of insulin. An acute treatment of 100 mg/kg of Alpha Lipoic Acid for one hour or chronic treatment (30 mg/kg for 10 days) produced a 50% improvement in glucose uptake in the skeletal muscles of the experimental animals. (Life Extension, 1996)

L Arginine

L-arginine is a semi-essential amino acid synthesized by the body from ornithine. It supports protein synthesis through its involvement in the transport and storage of nitrogen. L-arginine is important for proper physical performance because it is used by the body to produce creatine.

Other potential uses for L-Arginine include:

- For the immune system, it increases the size and activity of the thymus gland which is responsible for manufacturing T-lymphocytes.
- In the pancreas, it is used to release insulin.
- In the pituitary gland, it is a component of human growth hormone.
- In the liver, it assists in neutralizing ammonia.
- It is required in muscle metabolism where it helps maintain the nitrogen balance.
- In weight control, it facilitates the increase of muscle mass, while reducing body fat.

L-proline & L-lysine

L-proline is an important amino acid for maintaining youthful skin. It is also critical in the repair of muscle, connective tissue, immune function and tissue after injury.

L-lysine is concentrated in muscle tissue and is important in the absorption of calcium from the intestinal tract and in the formation of collagen. Collagen is an important body protein that is the basic matrix of connective tissue, skin cartilage and bone. There is some evidence that lysine may help prevent osteoporosis through enhancing the absorption and utilization of calcium.

Dr. Linus Pauling, twice the Nobel Prize winner for his work with vitamin C, discovered that *lipoprotein a* (or Lp(a)), a variant LDL cholesterol, has a receptor for lysine From this information, he theorized that specific nontoxic substances called Lp(a) binding inhibitors, such as lysine (and proline), prevent and even dissolve existing atherosclerotic plaque buildups. .

Pauling Therapy increases the concentration of the essential and nontoxic amino acid lysine (and proline) in the blood serum. His theory was *"the higher the concentration of free lysine and proline, in the blood, the more*

likely it is that Lp(a) molecules will bind with lysine, rather than the lysine strands that have been exposed by cracks in blood vessels or other lysine that has been attached to the Lp(a) already attached to the blood vessel wall."

The 1985 Nobel Prize in medicine was awarded for the discovery of cholesterol binding sites, referred to as "Lysine Binding Sites." A surprising body of experimental research supports Dr. Pauling theory. For best results, vitamin C should be used with these amino acids..

Suggested usage of Signa-Cell AM

Two capsules are recommended for most people. They are most effectively utilized by the body when they are taken on an empty stomach with water or juice in divided doses 30 to 45 minutes before breakfast or lunch. In rare instances, there may be slight gastric upset. In this case, reduce to one capsule and consumed with food.

Item # 6001 60 Capsules

References

Alternative Medicine, Linus Pauling on Heart Disease, Dec. 2002.

Biosent Carnitines, Providing Well Being Through Science. Sigma-tau Health Sciences, Tech Bulletin, 2002.

Colebank, Susan, Scavenger Hunt,The Antioxidants That Scavenge for Free Radicals also Improve our Quality of Life. Health Supplement Retailer, march 2001: 24-28.

Cronin, Joseph R., PhD., Acetyl-L-carnitine and Alpha Lipoic Acid - A Possible Antiaging Combination. Alternative and Complementary Therapies, Aug. 2002: 242-245.

DeFelice, Stephen L., M.D., The Carnitine Defense, a Nutraceutical Formula to Prevent and Treat Heart Disease, The Nations #1 Killer, Rodale Books, 1999.

Hass, Elson M., M.D. Staying Healthy with Nutrition, Celestial Arts, 1992.

Jordan, Karin G., M.D., PhD., Staying Young Forever. Life Extension Magazine, Dec., 1999.

Life Extension Magazine, Alpha Lipoic Acid for Diabetes, Atherosclerosis and Aging, March, 1996.

Mather, Timothy J. Ph.D., L-Carnitine - Nutrition for Neonates and Infants. New Hope Institute, March, 2001.

Passwater, Richard A, PhD., Turing up Metabolism, Vitamins, Minerals and Key Biochemicals can Aid in Cancer Prevention and Help Delay Signs of Aging, Whole Foods, Oct. 2002,:60-62.

Sigma-Tau Health Science, L-Carnitine Salts and Derivatives. Research Handbook, 2002.

Zdalnowicz, Martin M., Ph.D., Acetyl-L-carnitine's Healing Potential. New Hope Institute, Oct. 2001.