

LIFEPAK[®] NANO TECHNICAL OVERVIEW

LIFEPAK[®] NANO AND ITS COMPOSITION

What is lifepak[®] nano?

Lifepak[®] nano is a nutritional anti-aging program formulated to nourish and protect cells, tissues, and organs in the body with the specific purpose to guard against the ravages of aging. Lifepak[®] nano offers the highest bioavailability with a first-ever nanotechnology process and advanced levels of key anti-aging nutrients in a comprehensive formula.*

What makes lifepak[®] nano unique?

Lifepak[®] nano is the most scientifically balanced anti-aging supplement for adults with three scientific innovations: 1. superior bioavailability (*via* nanotechnology and liponutrients), 2. broad range cell and body protection with more than 60 antioxidants, and 3. key ingredient advances for heart and cell health benefits including resveratrol polyphenols and a new vitamin E blend.

What are the health benefits of lifepak[®] nano?

Lifepak[®] nano helps protect your health today and throughout your lifespan with superior benefits as an anti-aging program. This proprietary formula protects DNA and cells, nourishes and protects the brain, bolsters the immune system, supports cardiovascular health, helps regulate blood sugar metabolism, protects eye health, helps build strong bones, promotes joint function and mobility, helps maintain healthy skin tone and elasticity, helps protect against the affects sun radiation, and other anti-aging benefits.*

What is the recommended adult use?

Take two twin sachet packets daily. Take the contents of one (1) lifepak[®] nano twin sachet (5 capsules and 2 softgels) with eight (8) ounces of liquid with your morning and evening meals.

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How do lifepak[®] nano's nano-nutrients work?

Fat-soluble nutrients, like carotenoids and CoQ10, tend to cling together in the digestive tract, making them difficult to absorb. To enhance absorbability, individual molecules are separated using nano encapsulation. This process prevents molecules from clinging together so they are individually dispersed and more available for easy absorption. This superior bioavailability with new patent-pending CR-6 LipoNutrients is a first-ever formula to deliver Nano CoQ10 and nano-carotenoids along with other nutrients for maximum anti-aging benefit. And in the case of coenzyme Q-10, this process of nano-encapsulation increases bioavailability by 5-10 times.

What does CR-6 LipoNutrients[™] stand for?

Each serving of lifepak[®] nano is delivered in a convenient twin sachet packet; one side contains five dry capsules, and the other side contains two CR-6 softgel capsules. The meaning of the name *CR-6* stands for the six carotenoids (CR=carotenoid) present in the softgel capsule. In addition to the six carotenoids, Vitamins A and E are delivered along with essential omega-3's (equivalent in potency to a serving of MarineOmega). The name CR-6 LipoNutrients refers to all the contents of the softgel, all of which are fat-soluble nutrients; and all of which are enhanced through pre-fat-dissolved delivery, or enhanced with nanotechnology.

Who should take lifepak[®] nano?

Lifepak[®] nano is intended for adults (ages 18 and up) who are looking for the most advanced and comprehensive dietary health & wellness supplement. Lifepak[®] nano is ideal for individuals who were previously taking either LifePak[®] regular, LifePak[®] Prime, or LifePak[®] Women, in conjunction with MarineOmega. Due to lifepak[®] nano's unique delivery of certain antioxidant, it is also ideal for individuals who feel they are genetically predisposed to poor absorption of carotenoids. Also, persons prone to supplement-induced nausea may find that lifepak[®] nano's sources of minerals are better tolerated.

Will lifepak[®] nano help raise my Skin Carotenoid Score?

Carotenoids play a crucial role in supporting the entire antioxidant network, yet as fat soluble nutrients they are poorly absorbed, and a small percentage of the

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population is extremely challenged at absorbing these important nutrients (individuals who experience only slight increases in their SCS are known as *non-responders* due to their abnormally low ability to absorb carotenoids). Lifepak® nano includes nano-carotenoids to improve absorption of these *hard-to-absorb* antioxidants. Improved absorption has been shown to increase Skin Carotenoid Scores.

Do I still need to take MarineOmega™ if I take lifepak® nano?

Previous to the introduction of lifepak® nano, all LifePak family products were recommended to be taken with MarineOmega. Each serving of lifepak® nano delivers the same levels of EPA and DHA as found in a serving of MarineOmega. If you continue taking any LifePak family product other than lifepak® nano, it is still recommended that you take MarineOmega.

Why is it important to take lifepak® nano twice a day?

Lifepak® nano is a comprehensive supplement that contains a potent blend of essential micro- and macro-nutrients, as well as semi-essential nutrients shown to be generally beneficial to long-term health and well-being. It should be taken twice daily to provide your body with optimal saturation and absorption of vitamins and minerals. Twice daily delivery also provides your body 24-hour antioxidant protection of water soluble antioxidants that are flushed out of the body throughout the day.

What are the 60+ antioxidants in lifepak® nano?

All-trans-beta-carotene, 11-cis-beta-carotene, 13-cis-beta-carotene, vitamin A, buffered vitamin C, all 8 forms of natural vitamin E (d-alpha-tocopherol, d-beta-tocopherol, d-gamma-tocopherol, d-delta-tocopherol, d-alpha-tocotrienol, d-beta-tocotrienol, d-gamma-tocotrienol, d-delta-tocotrienol), selenium, copper, zinc, manganese, all-trans-lycopene, all-trans-alpha-carotene, cis-lycopene, all-trans-lutein, all-trans-astaxanthin, 9-cis-astaxanthin, 13-cis-astaxanthin, all-trans-zeaxanthin, 9 green tea catechins and glycosides [(+)-catechin (C), epicatechin (EC), epigallocatechin (EGC), epicatechin gallate (ECg), epigallocatechin gallate (EGCg), DL-Catechin (DL-C), Gallocatechin gallate (GCG), kaempferol glycoside, myricetin glycoside], 20 grape seed polyphenols (epicatechin gallate, catechin dimer, catechin dimer gallate, catechin trimer,

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catechin dimer digallate, catechin trimer gallate, catechin tetramer, catechin tetramer gallate, catechin pentamer, catechin trimer digallate, catechin tetramer digallate, catechin pentamer gallate, catechin hexamer, catechin pentamer digallate, catechin tetramer trigallate, catechin hexamer gallate, catechin pentamer trigallate, catechin hexamer digallate, catechin heptamer, and catechin heptamer gallate), quercetin, naringenin, hesperidin, 4 resveratrol polyphenols (trans-resveratrol, cis-resveratrol, trans-piceid, cis-piceid), novel krill flavonoid (not yet named), alpha-lipoic acid, N-acetyl-L-cysteine, coenzyme Q10.

What is the difference between lifepak® nano, LifePak®, LifePak® Prime, LifePak® Women, and LifePak® Prenatal?

Lifepak® nano has been formulated to meet the nutritional needs of all adults, ages 18-108 years (with the exception of pregnant women). Lifepak® nano delivers the benefits of LifePak®, LifePak® Prime, and LifePak® Women but with the exciting addition of nanotechnology and CR-6 LipoNutrients. CR-6 LipoNutrient softgels offer enhanced absorption for nutrients known to be poorly absorbed. Also, the CR-6 LipoNutrient softgels contain ultra-pure fish oils in amounts equivalent to a full serving of MarineOmega. A few ingredients that are available in LifePak® Prime (such as ginkgo and glucosamine), and Lifepak® Women (such as evening primrose oil and cranberry) are not offered in lifepak® nano, however most of the targeted benefits of these ingredients are provided through ingredients unique to lifepak® nano; those that are not can be achieved through separate Pharmanex products like Estera Cranberry.

Why should I take lifepak® nano instead of the combination of LifePak® and MarineOmega™?

Delivering the combined benefits of LifePak® and MarineOmega is only the first step of understanding Lifepak® nano. Lifepak® nano employs nanotechnology for enhanced absorption of nutrients known to be poorly absorbed. The nanotechnology process prevents molecules from clinging together so they are more available for easy absorption. This superior bioavailability with new patent-pending CR-6 LipoNutrients is a first-ever formula to deliver Nano CoQ10 and nano-carotenoids along with other nutrients for maximum anti-aging benefit.

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Does lifepak[®] nano conform to the 6S[®] Quality Process?

The combination of quality ingredients, qualified manufacturers, certified independent laboratory verification, and a continuous drive to supply leading-edge products ensures our representatives and consumers the highest quality products available in the industry. Lifepak[®] nano is guaranteed to contain no added sugar, salt, wheat, dairy products, artificial preservatives or colors. The vitamins and minerals used in Pharmanex products meet the requirements and guidelines established by the United States Pharmacopoeia (USP) and/or Food Chemicals Codex (FCC) where applicable. Every batch of lifepak[®] nano meets the USP XXV requirements for capsule disintegration. All ingredients are tested for purity, and where applicable, ingredients are certified pure by microbial testing, such as tests for Salmonella, E. coli, other coliforms, Staphylococcus aureus, total plate counts, yeasts, molds, and pesticide residues. Our manufacturers go through a detailed selection and certification process to assure their compliance with Good Manufacturing Practice (GMP) standards set by the Food and Drug Administration (FDA).

What is the best way to open the twin sachets?

Lifepak[®] nano comes in a convenient twin sachet packet, with a compartment for the dry capsules, and a compartment for the CR-6 softgels. The compartments can be opened separately, or for greater convenience: fold the twin sachet along the seal that separates the compartments. Once you have folded the twin sachet, the packet will be “doubled-up” allowing you to tear along the serrated edge of both ends of the packet. In this way you can open up both sachets with one tear.

NANOTECHNOLOGY

What is nanotechnology?

As applicable to nutrition, nanotechnology is the manipulation of nutrients at the molecular level to enhance their benefits to the body. A nanometer represents 1 billionth of a meter, and provides a useful unit for measuring ultra-small molecules. The application of nanotechnology employed by Pharmanex is a mono-molecular encapsulation where single molecules of important nutrients

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are embedded into single nanocapsule molecules. Since every single molecule of each nanoized-nutrient is wrapped in its own individual nanocapsule there is complete molecular dispersion of the fat-soluble nutrients. With complete molecular dispersion, the surface area of the nutrient is maximized as is its contact with the lining of the gastrointestinal tract. The nutrient is absorbed through the gut, and the encapsulating-molecule is left behind where it is degraded by digestive enzymes.

How does lifepak[®] nano improve delivery of certain fat-soluble vitamins?

While some nutrients in lifepak[®] nano have been enhanced through nanotechnology, yet others have been enhanced through their delivery in LipoNutrient form. Other fat soluble vitamins have been included as part of the CR-6 softgel capsules. Because these fat soluble nutrients are delivered in a matrix of essential omega-3 fatty acids, they are pre-dissolved for superior bioavailability.

What is unique about the nano-carotenoid blend?

Carotenoids play a crucial role in supporting the entire antioxidant network, yet they are poorly absorbed. Because carotenoids act as a first line of defense against external free-radicals they receive free radical hits first, thus sparing other antioxidant in the network. Lifepak[®] nano includes nano-carotenoids to improve absorption of these *hard-to-absorb* antioxidants. With greater absorption of carotenoids (made possible by nanotechnology) other network antioxidants are reserved to protect cell structures against internally produced free-radicals.

Which nutrients are in nano-form in lifepak[®] nano?

Nanotechnology is only one example of methods Pharmanex has employed to improve absorption of lifepak[®] nano's nutrients. The specific nutrients that have been enhanced with nanotechnology include those known to be poorly absorbed in the digestive tract, including beta-carotene, alpha carotene, astaxanthin, zeaxanthin, lycopene and CoQ10. These nutrients have been manipulated to enhance their bioavailability without altering their function as nutrients.

Why aren't all the ingredients in lifepak[®] nano in nano-form?

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Pharmanex scientists worked to identify molecules which are poorly absorbed and applied nanotechnology specifically to these nutrients. Most water soluble nutrients are easily absorbed, while the hydrophobic properties of fat soluble nutrients (such as carotenoids) make them difficult to absorb. Beyond nanotechnology, lifepak[®] nano employs other methods to enhance bioavailability, including liponutrients, chelated minerals and buffered vitamin C. Each of these nutrient forms were selected for their superior absorption properties.

How does lifepak[®] nano meet or exceed the requirements for a bona fide “nanotechnology” product

Lifepak[®] nano meets or exceeds federal requirements of a nanotechnology product. This term is defined by the FDA as research and technology or development of products regulated by FDA that involve all of the following: the existence of materials or products at the atomic, molecular or macromolecular levels, where at least one dimension that affects the functional behavior of the drug/device product is in the length scale range of approximately 1-100 nanometers; the creation and use of structures, devices and systems that have novel properties and functions because of their small size; and, the ability to control or manipulate the product on the atomic scale.

Is the Pharmanex nano process patented?

Nanotechnology is a term that applies to many fields of science, but Pharmanex is a pioneer in its nutritional application. The process of nano-encapsulating carotenoids is proprietary to Pharmanex and cannot be duplicated by any other company. This process is patent-pending.

HEALTH BENEFITS

What are the health benefits of lifepak[®] nano?

Lifepak[®] nano is formulated as a convenient dietary supplementation program promoting general health and well-being for a healthy lifestyle. As a result, lifepak[®] nano supplementation offers many more health benefits than ordinary multivitamins, health benefits which are important in maintaining a healthy lifestyle. Lifepak[®] nano addresses

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the following important health issues: common nutrient deficiencies, anti-aging benefits, cardiovascular health, bone structure and function, insulin function and normal blood glucose levels, immune function, and many others.

How does lifepak® nano target anti-aging?

Lifepak® nano contains 60+ antioxidants to address the symptoms of the normal aging process, including resveratrol, alpha-lipoic acid, vitamin C, vitamin E, folic acid, vitamin B12, flavonoids, mixed carotenoids, and other important micronutrients. Lifepak® nano is optimally formulated to provide comprehensive protection of cellular and mitochondrial DNA, as well as the body's lipids and proteins which are key determinants of the aging process. Many of these nutrients are delivered in forms enhanced by nanotechnology. Also lifepak® nano provides the anti-aging benefits of omega-3 fatty acids and krill oil. Long-term dietary supplementation with lifepak® nano can be expected to provide significant anti-aging benefits.

How does lifepak® nano support cardiovascular health?

Lifepak® nano addresses many aspects of cardiovascular health. Lifepak® nano is formulated to provide the recommended amounts of the key cardiovascular nutrients, such as vitamin E, vitamin C, carotenoids, flavonoids, vitamin B6, folate, vitamin B12, magnesium, and calcium. Thousands of scientific studies document the beneficial effects of individual antioxidant nutrients on cardiovascular health, and a number of studies indicated that combinations of antioxidant vitamins, carotenoids, and flavonoids are believed to be more effective than supplementation with any of these nutrients alone. (Smidt 1999, Manson 1993, Gey 1998, Anderson 1999, Mosca 1997)

Many clinical trials have been published to date, documenting omega-3 fatty acids' benefit to the cardiovascular system. The clinical studies have included short and long-term, placebo-controlled and comparative studies versus omega-6 fatty acids, and vitamin E. In these studies, omega-3 fatty acids have demonstrated significant associations with improved cardiovascular function. Several studies correlating fish consumption (providing omega-3 fatty acids) and longevity from cardiovascular health have shown that consumption of fish is associated with a substantial improvement in longevity (Thies 2003, Burr, 1989,

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Singh 1997, GISSI 1999). The American Heart Association (AHA) states: “Epidemiological and clinical trials have shown that omega-3 fatty acids reduce the risk of cardiovascular disease. Healthy people, people at high risk of CVD [cardiovascular disease] and patients with preexisting CVD all benefit. We recommend including omega-3 fatty acids in the diet mainly from fish and plant sources.” They continue on to say, “However, some people with high triglycerides (blood fats) and patients with CVD may benefit from more omega-3 fatty acids than they can easily get from diet alone. These people should talk to their doctor about taking supplements to reduce heart disease risk” (Kris-Etherton 2002). In the Harvard Health Professionals Follow-Up Study, the consumption of 1-3 servings of fish per week was associated with improved cardiovascular health (Connor 1997).

Carotenoids are partly responsible for a number of well-documented health benefits of diets rich in fruits and vegetables, including eye health, protecting skin from ultraviolet radiation damage, cardiovascular health, and prostate health (Smidt 2004). Carotenoids other than β -carotene appear to have profound cardiovascular health benefits (Arab 2000, Rao 2000). Lycopene helps protect LDL from oxidation, and α -carotene and lutein may be protective as well (Agarwal 1998, Chopra 2000, D’Odorico 2000, Kontush 1999, Irabarren 1997, Suter 2000). Large epidemiological studies suggest that dietary flavonoid intake from fruits, vegetables, tea, grape juice, and red wine is positively associated with cardiovascular health. (Hertog 1993, Hertog 1995, Knekt 1996, Keli 1996, Yochum 1999, Schramm 1998)

How does lifepak® nano improve bone nutrition?

Lifepak® nano addresses bone health with a comprehensive array of bone nutrients, all present in nutritionally significant amounts: calcium, magnesium, vitamin D, vitamin K, boron, and silicon. Calcium supplementation can promote healthy bone formation in young adults, and support healthy bone integrity in the elderly, and help protect against long-term concerns with bone strength (Teegardin 1994, Lee 1995, Welten 1995, Renner 1994, Reid 1995, Chiu 1999, Looker 1993, Power 1999, Reid 1998). Lifepak® nano delivers a special form of calcium— calcium malate, which has been shown to offer superior bioavailability, and be better tolerated by individuals prone to supplement-

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induced nausea. As the second most abundant bone mineral, magnesium appears to be equally important for bone health as calcium, especially as marginal or inadequate magnesium intake is a significant concern in the U.S. (Sojka 1995, Stendig-Lindberg 1993, Durlach 1998). There are a number of clinical trials documenting the benefits of supplemental vitamin D for maintaining normal bone health and calcium metabolism, especially in the elderly (Torgerson 1995, Ooms 1995, O'Brien 1998, Kaufman 1995) Although vitamin D is produced in the skin upon sunlight exposure, marginal vitamin D status is common especially in the elderly living in the northern latitudes of the United States and Canada (Bouillon 1987, Gloth 1995, Kessenich 1996, Holick 1995). Lifepak® nano provides three other bone nutrients that are not typically found in other multivitamin/mineral supplements: vitamin K, boron, and silicon.

How does lifepak® nano support insulin and blood glucose metabolism?

Lifepak® nano provides high levels of antioxidant vitamins C and E, and the presence of significant amounts of alpha-lipoic acid, magnesium, zinc, and chromium, make lifepak® nano an appropriate dietary supplement for people with concerns about their blood glucose levels. Clinical observations showed that the supplemental chromium alleviated concerns related to blood glucose levels in individuals deficient in chromium (FNB 1989, Freund 1979, Jeejeebhoy 1977, Brown 1986, Jeejeebhoy 1999). It is now generally accepted that chromium acts as a cofactor for insulin (Mertz 1993, Anderson 1998). Inadequate chromium nutrition appears to be widespread in the United States and other industrialized countries, and may affect as much as 90 percent of the U.S. population (Anderson 1985). Zinc may also promote normal insulin function by a more direct mechanism (Chausmer 1998, Brun 1995) Zinc deficiency is also very common in people with atypical insulin function and is attributed largely to poor dietary intake and high urinary excretion (Chausmer, 1998, el-Yazigi 1993, Blostein-Fujii 1997, Honnorat 1992). Antioxidant status is often low in patients with abnormal glucose metabolism, and supplementation with antioxidant nutrients has resulted in significant nutritional benefits (Maxwell 1997, Nuttall 1999, Cunningham 1998).

How does lifepak® nano improve immune function?

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Since the immune system depends on adequate nutritional status of many vitamins and minerals, it is expected that lifepak® nano effectively promotes healthy immune function in many ways. Vitamins A, C, E, and B6, and the minerals zinc and selenium, and omega-3 fatty acids all have important influences on the immune system, and supplementation with these nutrients has been shown to improve immunity in populations at risk of deficiencies (Chandra 1997, Erickson 2000, Lesourd 1997, Bogden 1994). Vitamin A is essential for maintaining a normal immune response (Semba 1994, FNB 1989). Several papers have implicated the role of omega-3 fatty acids in optimal immune function, as an imbalance in fatty acid nutrition may cause sub-optimal immune function (Simopoulos 1999, Simopoulos 1991, Calder et al 2002).

What are the brain health benefits of lifepak® nano?

Lifepak® nano provides clinically significant levels of omega-3 fatty acids, which have been shown to provide important brain health benefits. An association between the brain content of DHA, mental capacity, and mental health has been observed in numerous scientific studies. The ratio of membrane omega-3 to omega-6 fatty acids can be modulated by dietary intake, and this ratio influences neurotransmission and prostaglandin formation, processes that are vital in the maintenance of normal brain function (Haag 2003). Fish oil has been shown to increase nitric oxide synthase, a mediator of neurotransmission in the brain. Children with low levels of omega-3 fatty acids have been shown to have a lower overall mental capacity, especially in solving mathematical problems, and have difficulty sleeping. Research has shown that DHA and other long chain fatty acids are associated with improved visual and cognitive development (Willatts 2002). DHA is also thought to be an extremely important fatty acid for brain function (Michael 1993). In addition, phospholipids, naturally found in krill oil, are important in brain function (Hirata 1980; Amaducci 1991). Combining Krill oil with omega-3 fatty acids from fish oil provide unique benefits by providing a significant dosage of EPA and DHA from fish oil along with the unique brain health benefits provided by krill phospholipids.

Does lifepak® nano provide joint health benefits?

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Lifepak® nano provides omega-3 fatty acids, which can help promote joint health and mobility according to 13 double-blind placebo-controlled studies involving a total of over 500 people. Consumption of broiled or baked fish with two or more servings per week, but not other types of fish, was associated with a significant improvement in joint mobility and flexibility. Another study found that dietary supplementation of omega-3 fatty acids from fish oil (40 mg/kg/day) combined with a low intake of omega-6 fatty acids (<10 g/day) resulted in a significant increase in EPA in plasma and monocyte lipids, and improvements in clinical status in participants (Volker 2000).

What other health benefits are provided by lifepak® nano?

Lifepak® nano helps maintain healthy eyesight, promotes healthy teeth and gums, supports weight management efforts, promotes skin function and protection, supports energy metabolism, and helps maintain mental performance.

INGREDIENT INFORMATION

Are the ingredients in lifepak® nano substantiated by clinical studies?

There are over 200,000 published studies on the antioxidants in lifepak® nano and over 800,000 published studies on its comprehensive list of 60+ ingredients. Furthermore, LifePak® has been subjected to several clinical studies that have demonstrated specific antioxidant and cardiovascular benefits from regular and consistent use of LifePak®. Two double-blind, placebo-controlled clinical studies concluded that LifePak® significantly increased antioxidant status, and decreased LDL oxidizability in healthy non-smokers consuming typical U.S. diets. (Smidt 1999, unpublished study)

What carotenoids does lifepak® nano provide?

Carotenoids are a class of phytonutrients with many important nutritional and biochemical functions in mammals. Carotenoids are partly responsible for a number of well-documented health benefits of diets rich in fruits and vegetables, including eye health, protecting skin from ultraviolet radiation damage, cardiovascular health, and prostate health (Smidt 2004). Carotenoid intakes in the U.S. population are considered low, and reflect low fruit and vegetable

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consumption (Lachance 1988). Lifepak® nano provides a balanced carotenoid combination in amounts similar to those provided by diets high in fruits and vegetables. The specific carotenoids in lifepak® nano are beta-carotene, alpha-carotene, lycopene, lutein, zeaxanthin and astaxanthin.

What is astaxanthin?

Astaxanthin is the carotenoid-antioxidant responsible for the red/pink color in salmon, lobster, shrimp, and krill. Astaxanthin is delivered from two sources in lifepak® nano: krill oil, and an algae source (*Haematococcus pluvialis*). As with all carotenoids, astaxanthin is mainly produced by plant life, and enters the animal food-chain only as they consume plant sources. Compared to beta-carotene, astaxanthin has two extra functional groups which give astaxanthin an extraordinary antioxidant capability.

What is zeaxanthin?

Zeaxanthin is an important carotenoid for the protection of the retina in the eye. It found in many yellow to orange fruits and vegetables. It is also present in dark green leafy vegetables such as spinach, however is not visible due to the green pigment chlorophyll. Together with lutein, zeaxanthin acts as an antioxidant for the retina by filtering the harmful effects of blue and near ultra violet light. Because zeaxanthin is less abundant in our diets than lutein, our bodies attempt to compensate by converting dietary lutein into meso-zeaxanthin. This conversion of lutein to zeaxanthin becomes less effective as we age, providing good evidence for zeaxanthin supplementation. Lifepak® nano provides zeaxanthin enhanced by nanotechnology for superior bioavailability.

What flavonoids does lifepak® nano provide?

Flavonoids form an important class of antioxidant phytonutrients with antioxidant and cardiovascular health benefits (Bravo 1998). It is estimated that there are over 600 different flavonoids present in foods and beverages. Some research shows that different flavonoids may have synergistic effects when taken in combination (Pignatelli 2000). Estimates of average daily flavonoid consumption in industrialized nations vary from 20 to 100 mg per day (Justesen 1997, Dragsted 1997, Linseisen 1997). Lifepak® nano delivers an impressive

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220 milligrams of flavonoids daily, including green tea catechins, citrus bioflavonoids, quercetin, grape seed extract and resveratrol.

What are resveratrol polyphenols?

Polyphenol compounds found in the skins of red grapes to which researchers attribute the health benefits of red wine. Scientists continue to identify the link between this powerful antioxidant and healthy lifestyles enjoyed throughout the Mediterranean region. Resveratrol supports healthy aging in many body systems as an antioxidant, but beyond its antioxidant functions resveratrol has been studied for its effects on the cardiovascular system and brain tissue as it relates to the normal aging process.

How is the vitamin E source different than previous LifePak® products?

Lifepak® nano delivers an updated vitamin E complex blend according to latest scientific research. The large body of scientific evidence supporting alpha-tocopherol remains unchallenged, with the vast majority of studies supporting its cardiovascular and antioxidant benefits. However, within the recent five years, research on the other tocopherols, especially gamma-tocopherol, has yielded compelling evidence of previously overlooked health benefits. Moreover, studies indicate that lower doses of alpha-tocopherol can be more effective than high doses, when combined with balanced doses of gamma-tocopherol and the other tocopherols. Because non-alpha-tocopherols (beta, gamma, delta) are not expressed in IU units, Lifepak® nano lists these separately also as a result, lifepak® nano has a slightly decreased alpha-tocopherol level, but higher levels of the other tocopherols yielding a much more powerful total vitamin E blend.

What is unique about the new source of calcium?

Lifepak® nano offers a new calcium complex with calcium malate— a more absorbable form of calcium, and is better tolerated by individuals prone to supplement-induced nausea. Because calcium malate is more bioavailable, lower amounts are required to achieve a similar effect as compared to other forms of calcium.

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What is NanoCoQ10? Do I need to take NanoCoQ10 separately if I take lifepak® nano?

NanoCoQ10 is an enhanced form of Coenzyme Q10, an antioxidant whose primary functions are cellular energy production (metabolism) and free radical scavenging. Coenzyme Q10 helps to maintain vitamins C and E in their reduced (active) state. In humans, coenzyme Q10 levels reach their peak in most tissues by the age of 20 and then fall slowly thereafter. Lifepak® nano's NanoCoQ10 has been shown in preliminary studies to have increased bioavailability by 5-10 times! Individuals looking for benefits of higher amounts of CoQ10 may decide to take additional NanoCoQ10 in the form of the stand-alone product.

Why were soy isoflavones not included in the lifepak® nano formula?

Pharmanex continues to offer soy isoflavones in LifePak® Prime, LifePak® Women, Bone Formula, and Estera Phases I, II, and III. In these products soy isoflavones offer cardiovascular benefits—and to women they provide hormone support. Some individuals are looking for isoflavone-free supplements and so lifepak® nano provides cardiovascular benefits from resveratrol, while the hormone support benefits for women can be obtained from Estera products and Bone Formula.

What is the role of omega-3 fatty acids?

Lifepak® nano is an excellent source of essential omega-3 fatty acids typically lacking in people's diets. Omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are important for normal immune function, cardiovascular health, joint mobility, brain function, and skin health. Omega-3 fatty acids are building blocks for immune mediators and regulate thousands of metabolic functions through prostaglandin pathways

Clinical studies have shown that omega-3 fatty acids from fish oil and krill oil:

- Support cardiovascular health. Epidemiological and clinical trials have shown that people, who consume omega-3 fatty acids, maintain good cardiovascular health (Kris-Etherton 2002, Connor 1997).
- Promote joint health and mobility (Simopoulos 1991; Kremer 1996; Kremer & Robinson 1991; Kremer et al 1987);

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- May be helpful in boosting skin protection against UV rays and photoaging (Rhodes et al 2003; Rhodes et al 1995; Rhodes et al 1994, Jackson 2002; Boelsma et al 2001);
- Promote normal DHA content in the brain, supporting mental capacity and mental health. The ratio of membrane omega-3 to omega-6 can be modulated by dietary intake, and this ratio influences neurotransmission and prostaglandin formation, processes that are vital in the maintenance of normal brain function (Haag 2003).

What is Krill Oil?

Euphasia superba, commonly known as krill, are small shrimp or prawn-like crustaceans found in oceans off the West coast of Vancouver Island, Russia, Ukraine, Antarctica, and Japan. Neptune Krill Oil™ is marine oil offering a unique and natural combination of phospholipids high in EPA and DHA, potent antioxidants such as vitamins A, E and astaxanthin, and omega-3 and omega-9 (oleic) fatty acids.

What is the source of the omega-3 fatty acids in CR6 LipoNutrients?

MarineOmega™ provides the highest quality omega-3 fatty acids from fish oil and krill oil. The fish oil is derived from sardines, salmon, mackerel, and anchovies. Krill oil is derived from *Euphasia superba*, which are small shrimp or prawn-like crustaceans.

BACKGROUND INFORMATION

What are typical nutrient deficiencies in the adult population?

Large nutrition surveys have consistently shown that inadequate intakes of essential vitamins and minerals are common in the United States and other industrialized countries.^{3–6} The Continuing Survey of Food Intakes by Individuals (CSFII) conducted by the U.S. Department of Agriculture (USDA) in 1994–96 showed that most people do not meet the Recommended Dietary Allowances (RDAs) for essential vitamins and minerals (USDA 1996). The most common nutrient deficiencies appear to be for the antioxidant vitamins A and E, vitamin B6, the bone minerals calcium and magnesium, and

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the minerals iron—particularly for women— and zinc (USDA 1996). A large number of other studies document common nutrient deficiencies of vitamin D, thiamin, riboflavin, vitamin B6, folate, vitamin B12, calcium, magnesium, zinc, copper and chromium (Delvin 1988, Nichols 1994, Skelton 1989, Smidt 1991, Tiidus 1989, Toh 1994, van der Wielen 1996, Haller 1991, Kant 1990, Selhub 1993, Lowik 1990, Fleming 1994, Prasad 1995, Small 1994, Pennington 1989, Abdulla 1989, Anderson 1993, Kant 1991). These common deficiencies in vitamin and mineral intakes can be attributed to the consumption of unbalanced diets that are low in fruits and vegetables^{65, 66} and rich in energy-dense, nutrient-poor foods (Kant 1991, Breslow 1997, Kant 1994). For example, an analysis by Block et al. of the National Health and Nutrition Examination Survey (NHANES II) data revealed that 41 percent of the population had no fruit on the survey day, only one fourth had a fruit or vegetable rich in vitamin A or in vitamin C, and only 10 percent consumed the recommended five servings of fruits and vegetables (Block 1991).

Researchers from Harvard Medical School and the Harvard School of Public Health have joined a growing list of scientific experts who recognize the benefits of vitamins by stating in a landmark review published in the June 19 2002 issue of *The Journal of the American Medical Association* that “all adults should take a multivitamin daily” (Fletcher 2002). The review suggests that suboptimal intake of some vitamins, above levels causing classic vitamin deficiency, is a risk factor for long-term health concerns and is common in the general population, especially the elderly. Most people do not consume an optimal amount of all vitamins by diet alone, leading the authors to point out that most supplements are a convenient and affordable way to bridge the nutrition gap.

Aside from eating more balanced diets rich in fruits and vegetables, lifepak® nano supplementation ensures meeting the RDAs for all vitamins and minerals. The amounts of vitamins and minerals included in LifePak® nano were chosen not only to prevent vitamin and mineral deficiencies, but also to correct any pre-existing deficiencies with regular use.

What is an antioxidant network?

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There are hundreds of different antioxidants that can help fight free radicals and reactive oxygen species. Researchers have found that the body utilizes a broad range of antioxidants that work together to provide the body with optimal free radical protection. These antioxidants work synergistically to protect all of the delicate DNA tissue in the body from free radical attack. It has been found that if just one or two of these antioxidants are deficient that other antioxidants in the body are not able to function properly. Moreover, because of this antioxidant network, humans have a need to supplement a broad range of antioxidants into the diet, as found in LifePak® nano's 60+ antioxidants.

Why are omega-3 fatty acids important?

Omega-6 and omega-3 fatty acids are two of the forty-nine essential nutrients. As essential nutrients they cannot be synthesized by the body, but must be ingested directly in the form of foods or dietary supplements. Essential fatty acids are necessary for normal growth, healthy skin, circulation, nerves, and metabolism. However, in Western society, the ratio of intake of omega-6 fatty acids, found in common plant oils, to the intake of omega-3 fatty acids, found in fish oil, (omega-6/Omega-3) is too high (Simopoulos 1999; Kris-Etherton 2000), and can lead to the formation of excess arachidonic acid and potentially harmful eicosanoid products in the body (James 2000). Science now supports the importance of reducing the intake of omega-6 fatty acids, such as linoleic acid, and increasing the intake of omega-3 fatty acids in the diet of adults and newborns for optimal brain and cardiovascular health and function (Simopoulos 1999).

What is a fatty acid imbalance?

Based on estimates from studies, humans evolved on a diet that consisted of a roughly equal ratio of omega-6 to omega-3 fatty acids, but the current human diet has drifted a long way from that standard. Today, a significantly higher level of saturated fats and vegetable oils containing omega-6 fatty acids are consumed, whereas the intake of omega-3 fatty acids (primarily from fish and wild game) has decreased by 80% during the last 80 years. Currently the ratio of omega-6 to omega-3 in the American diet ranges from 20:1 to 30:1 in many Western countries, to 4:1 in Japan – with ratios grossly in favor of omega-6 fatty acids (Simopoulos 1996; Chapman 1992; Ristic & Ristic 2003).

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Many papers have implicated the role of omega-3 fatty acids in cardiovascular health, optimal immune function, and optimal brain function. (Connor & Connor 1997; Davidson et al. 1997; Nair et al. 1997; Simopoulos 1999; Harris et al 1997; Burr & Fehily 1991; Burr et al 1989; Radack et al 1989; Endres et al 1997; Simopoulos 1991; Sperling 1991; Endres S et al 1991; Kremer 1996; Belluzi et al 1996; Kremer & Robinson 1991; Kremer et al 1987; Calder et al 2002; Nkondjock et al 2003; Tapiero H et al 2002).

SAFETY

Is this product safe?

Each ingredient in lifepak® nano is present in amounts that are documented to be safe for long-term supplementation. The daily amounts of all vitamins and minerals are well below the No-Observed Adverse Effect Levels (NOAEL) established by the Council for Responsible Nutrition (CRN) in 1997⁴¹⁶ and the Upper Limits (UL) established by the Food and Nutrition Board of the National Research Council (FNB 1997). The other nutrients of lifepak® nano, i.e., the phytonutrients, are added in amounts that can be obtained from diets high in fruits and vegetables (5–10 servings/day) or other commonly consumed foods and beverages. All of the phytonutrient extracts used in lifepak® nano are documented to be safe and non-toxic. These extracts have been studied in humans at daily intakes similar or higher than those supplied by lifepak® nano and no significant side effects were reported.

Additionally, fish oil is a food constituent. Adverse effects with diabetics, such as increased plasma glucose, LDL cholesterol, and glycosylated hemoglobin have been observed with large, perhaps excessive doses of omega-3 fatty acids, in the range of 4-10g/day. Lifepak® nano follows the strictest quality control standards set by the FDA under the Good Manufacturing Practices (GMP). These standards are established to protect the consumer from potentially harmful compounds.

Are there any side effects?

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There are no known side effects of lifepak[®] nano or any of its ingredients at the recommended usage levels. A clinical study of LifePak[®] in 46 healthy subjects conducted under FDA Good Clinical Practices guidelines revealed no adverse effects attributable to LifePak[®] (Smidt 1999). Similar observations were made in another, similar clinical study of LifePak[®] in 140 healthy subjects (unpublished results). The most common side effects observed with fish oil are complaints of fishy taste. At relatively higher doses of fish oil, gastrointestinal complaints, including loose stools have been reported.

Are there any contraindications or drug interactions?

If you are pregnant or lactating, or taking a prescription medication including high-dose aspirin therapy or anticoagulants, consult a physician prior to use. Discontinue use of this product two weeks prior to and after surgery. Many drugs can alter the metabolism and bioavailability of vitamins and minerals, and likewise—although much less frequently—some nutrients may also affect drug pharmacokinetics (Thomas 1995, Matsui 1997). For example, antituberculous drugs such as INH and cycloserine interfere with vitamin B6 metabolism and may also produce a secondary niacin deficiency. Oral contraceptives interfere with the metabolism of folic acid, ascorbic acid, and riboflavin. Anticonvulsants can act as folate antagonists and precipitate folic acid deficiency, and supplementation with folate has been recommended along with anticonvulsant therapy. Cholestyramine therapy has been associated with malabsorption of vitamins, such as vitamins K and D, and folic acid. Multivitamin supplementation has been recommended to avoid such adverse effects of drugs on nutrient metabolism. An excellent recent review of drug-nutrient interactions was prepared by Thomas (1995).

Are there any known drug interactions?

People on high-dose aspirin therapy, or those taking anticoagulant drugs or other medications should consult a physician before taking this or other dietary supplements.

KEY STUDIES

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