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Resveratrol, Quercetin and Grape Polyphenols: Red Wine Components Enhance Heart Health and Longevity

By Chris D. Meletis, ND and Jeffrey Reinhardt, MSc

Resveratrol is the best known health promoting molecule in red wine¹ and has been studied by scientists investigating its effects on genes as well as the heart, breast, prostate, uterus, and immune system. In addition, recent studies show that resveratrol sustains healthy nerves and important brain functions including cognitive processes.²⁻⁴

In various epidemiological studies and clinical trials, consumption of resveratrol, quercetin and other red wine components have been associated with a reduced risk of heart disease and improved cardiovascular

health. *In vitro* and animal studies also have shown that red wine components can influence various factors associated with breast, prostate and lung health, and can reduce the free radical damage that occurs during influenza virus infection. In fact, quercetin, red wine polyphenols and resveratrol provide important synergistic benefits for the heart.

Heart Health

Resveratrol is a plant protective phytoalexin produced by grapes, mulberries, peanuts and soy beans, and is found in honeybee hives,

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Annatto Tocotrienols: Vitamin E Component Dramatically More Effective at Supporting Heart Health

by Barrie Tan, PhD and Anne Mueller, MSc

Vitamin E is often thought of as a single entity. However, it is a mixture of both tocotrienols and tocopherols, two forms of the same vitamin. Scientists have found that although both tocotrienols and tocopherols are similar, they work differently in the body. In fact, the newest research indicates that even though both forms possess antioxidant activity, tocotrienols are superior to tocopherols in ways essential to good health. Furthermore, evidence indicates

that tocotrienols are absorbed better than tocopherols¹ and that alpha-tocopherol (the most common form of Vitamin E supplementation worldwide) blocks absorption of tocotrienols,² compromising tocotrienols' ability to maintain healthy cholesterol levels and sustain the integrity of nerves.

In this article, we will discuss the differences between tocopherols and tocotrienols and explain why a special form of delta-tocotrienol derived from the Annatto plant

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Resveratrol

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red wines such as Pinot Noir, Itadori tea and various medicinal herbs such as Japanese Knotweed (*Polygonum cuspidatum*). This compound occurs in two conformational forms – cis and trans-resveratrol. Trans-resveratrol is the preferred functional form. The most effective trans-resveratrol is one that is exceptionally high quality, extracted from *Polygonum cuspidatum* in a process that results in very low levels (1 percent or less) of undesirable cis- isomers. It is further enzymatically hydrolyzed to remove the glycosides (naturally-occurring sugar molecules), since the *aglycone* (sugar-free) form of trans-resveratrol is more efficiently absorbed. Accelerated stability studies performed with our trans-resveratrol demonstrate excellent stability over its projected two-year shelf life.

Trans-resveratrol is thought to improve heart health in a number of ways. Laboratory experiments *in vitro* and studies in animals have shown that trans-resveratrol can stop blood platelets from sticking together (platelet aggregation). In one study, scientists investigated the effects of resveratrol and red wine on aggregation of platelets isolated from healthy male volunteers.

The researchers induced platelet aggregation in blood from healthy subjects and determined that trans-resveratrol signifi-

cantly inhibited the sticking together of blood platelets. Researchers also induced platelet aggregation in rabbits with high cholesterol and found that when trans-resveratrol was given to the rabbits, the platelets did not stick together.⁵ Since sticky platelets are tied to increased risk of heart attack, stroke and blood clots throughout the body, this is a significant finding in regards to life-threatening risk factors.

According to the researchers, “These results suggest that trans-resveratrol can inhibit platelet aggregation both *in vitro* and *in vivo*, which conceivably could be one of the mechanisms by which this red wine polyphenol exerts its cardioprotective effects.”

Another of trans-resveratrol’s interesting cardiovascular implications is its ability to enhance angiogenesis, the development of new blood vessels, in order to help feed the heart during periods of oxygen deprivation (ischemia). The formation of new blood vessels caused by trans-resveratrol restores the blood supply to the ischemic area, preventing heart cell death and abnormal changes to the heart.⁶

In a study of 24 pre- and 20 postmenopausal women, researchers randomly assigned the subjects to receive either a placebo or grape powder rich in trans-resveratrol, quercetin and other polyphenols for four weeks. After a 3-week washout period, the subjects given the grape powder were switched to a placebo and the subjects receiving the placebo then received the grape powder. In both the pre- and postmenopausal women, concentrations of plasma triglycerides, another cardiac risk factor, dropped by 15 and 6 percent respectively after supplementation with the grape polyphenols. In addition, plasma LDL cholesterol and apolipoproteins B and E levels were lower after supplementation with the grape powder. In addition, whole-body oxidative stress was significantly reduced after supplementation with the grape powder. When subjects were taking the grape powder, the levels of plasma tumor necrosis factor-alpha, which plays a major role in the inflammation process, were lower.⁷ These results led the researchers to conclude that grape polyphenols, through alterations in lipoprotein metabolism, oxidative stress, and inflammatory markers, “beneficially affected key

risk factors for coronary heart disease in both pre- and postmenopausal women.”

In another study, red grape polyphenol extract containing quercetin, trans-resveratrol and other polyphenols improved blood flow in the arteries of male patients with coronary heart disease.⁸

Anti-Inflammatory Actions

Not only are trans-resveratrol, quercetin and other red wine polyphenols powerful antioxidants, they also exert a strong anti-inflammatory effect. They appear to accomplish this by inhibiting nuclear factor-kappa beta (NF-kappaB), a protein with a pivotal role in controlling cell signaling in the body under certain physiological and pathological conditions. Among other functions, NF-kappaB controls the expression of genes encoding the pro-inflammatory cytokines (proteins produced by white blood cells), chemokines (cytokines that assist in destroying invading micro-organisms) and immune receptors, all of which play critical roles in controlling most inflammatory processes. NF-kappaB is so important in controlling inflammation that over the last decade researchers have spent a great deal of time identifying compounds that interfere with the NF-kappaB pathway in the hopes of finding agents useful in inflammatory diseases such as arthritis, asthma and autoimmune conditions. Recently, researchers have discovered that trans-resveratrol, quercetin and other polyphenols found in red wine may inhibit the NF-kappaB pathway.⁹

These same red wine compounds inhibit expression of another important marker of inflammation and a risk factor for heart disease—C-reactive protein (CRP). Recent research has found that quercetin and trans-resveratrol can, in a dose-dependent manner, suppress the expression of CRP that occurs after the activation of inflammatory cytokines.¹⁰

Conclusion

Trans-resveratrol is a multifunctional modulator of numerous, complex cellular signaling pathways, which regulate vital cellular processes such as cell growth, apoptosis or programmed cell death, ischemic heart disease and thrombosis, insulin resistance and diet-induced obesity,

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Resveratrol and Life Extension

Despite centuries of explorations, the search for plants or other remedies that effectively and reliably extend life span has produced no miraculous “fountain of youth” discoveries. Over the last 20 years, medical scientists in the U.S. and in France, Japan and China confirmed that a low calorie, nutritionally balanced diet not only contributes significantly to sustained good health but also increases longevity in mice, rats, primates, yeast, round worms and fruit flies. These observations led scientists to search for “longevity genes.” Once triggered by environmental cues, the longevity genes “switch on” and induce defensive changes at the cellular level, such as slowing metabolism and enhancing cellular respiration to help the body adapt to a more beneficial survival program.

Researchers have found a family of genes, called sirtuins, produced by almost all life forms—from single celled organisms, to plants and mammals—during times of stress, such as famine (or caloric restriction). Sirtuins (silent information regulator proteins) are known to act as guardian genes that protect cells and enhance cellular survival. The human sirtuin, SIRT-1, for example, has been shown to suppress the p53 enzyme system normally involved in suppressing tumor growth and instigating cell death (apoptosis). By suppressing p53 activity, SIRT-1 prevents the cycle of premature aging and apoptosis normally induced when cellular DNA is damaged or stressed, thus giving cells enough time to repair any damage and prevent unnecessary cell death. A second sirtuin found in yeast, SIR2, has also been shown to become activated when placed under stress. SIR2 has been shown to increase DNA stability and speed cellular repairs, while increasing total cell lifespan. Essentially, sirtuins buy cells time to repair damage.¹⁻²

Caloric restriction triggers the activation of sirtuins, one of the mechanisms by which caloric restriction extends lifespan. Therefore, researchers wondered if there was another way to activate sirtuins in order to extend longevity. Researchers discovered that of a number of plant compounds tested, the most potent activator of sirtuins was resveratrol. Yeast treated with resveratrol lived for an average of



38 generations, as compared to only 19 generations for untreated yeast.³

The combination of resveratrol and Sirt1 stimulates a number of stress-modifying and life-extending processes including apoptosis, immune defense mechanisms, neuronal protection and metabolic optimization in liver, muscle and fat cells. Resveratrol has other actions, including stimulation of ATP production in mitochondria of mice and modulation of insulin growth factor 1 (IGF-1), improves insulin sensitivity, mitigates against obesity and minimizes the development of fatty livers in mice fed a high-fat diet.

In one animal study, researchers found that mice given resveratrol significantly increased their aerobic capacity, as evidenced by their increased running time and consumption of oxygen in muscle fibers. The animals also experienced improved mitochondrial function. Diminished mitochondrial function and aerobic capacity are associated with reduced longevity. Another interesting finding of the study was that resveratrol protected mice against diet-induced obesity and insulin resistance.⁴

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The President's Desk

Science-Backed Supplements

We take great pride in using the latest science as a springboard for formulating nutritional supplements. Our research and development team constantly search the medical literature for information about ingredients that have demonstrated the most impressive effects.

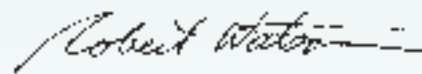
Three of our newest products confirm our dedication to science-backed nutritional supplements. I am especially excited about our new tocotrienols product. As you will see from the article in this newsletter, a special form of tocotrienols derived from the Annatto plant contains virtually no tocopherols. This is important because tocopherols counteract the cholesterol-lowering ability of tocotrienols.

Fucoidan, a seaweed component that can improve immune and cardiovascular health, also joins our product line this month. Our fucoidan source is sustainably harvested from pristine coastal waters of Nova Scotia ensuring a product free of heavy metal contaminants. This material is further extracted through an aqueous method to ensure maximum bioavailability, which requires less milligrams per capsule than fucoidan from Asian sources. You can read about this nutritional support from the sea in this newsletter.

Another new product is our high-dose resveratrol. In keeping with the latest findings in the medical literature, which show that higher levels of resveratrol can improve longevity and support cardiovascular health, we have developed a stable high-dose resveratrol product. The addition of quercetin and red wine polyphenols further supports the health-promoting benefits of resveratrol.

As with all our supplements, we never compromise quality in order to deliver a product at a lower price. Rest assured, our fucoidan, resveratrol and tocotrienols are sourced from only the finest suppliers who meet our highest standards.

This is an exciting time at our company. In the coming months you will see other new products and reformulations based on what our science team is reading in the medical literature. After all, research is our middle name.



Robert Watson
President/CEO

Tocotrienols

Continued from front page

can play an important part in maintaining cardiovascular health

Supporting Healthy Cholesterol Levels

As mentioned above, tocopherols do not have tocotrienols' cholesterol-lowering ability. In fact, alpha-tocopherol lessens or interferes with the cholesterol-lowering action of tocotrienols.³ Most vitamin E supplements contain primarily tocopherols (especially alpha-tocopherol) and only traces of tocotrienols. This is counterproductive in light of what we know about tocopherols inhibiting tocotrienols' absorption and the fact that large clinical studies on alpha-tocopherol's benefits to cardiovascular health have been equivocal.

Effective cholesterol-lowering preparations consist of less than 15-20 percent alpha-tocopherol and more than 60 percent gamma- and delta-tocotrienol, whereas less effective or ineffective preparations consist of more than 30 percent alpha-tocopherol and less than 45 percent of gamma- and delta-tocotrienol. In clinical studies, high alpha-tocopherol supplements did not contribute to cholesterol lowering,⁴⁻⁵ whereas supplements containing low amounts of alpha-tocopherol and high amounts of gamma- and delta-tocotrienol led to a significant decrease in total and LDL cholesterol.⁶⁻⁷

Animals consuming diets supplemented with gamma- and delta-tocotrienol showed the greatest cholesterol decrease (32 percent total cholesterol and 66 percent LDL cholesterol), whereas alpha-tocopherol had no effect on cholesterol lowering. In this study, HDL/LDL cholesterol ratios improved by 123-150 percent.⁸

In humans, two open studies² measured fasting blood lipids before and 2 months after supplementation with annatto tocotrienols (75 mg/day). In both groups, total cholesterol levels dropped 13 percent, whereas LDL cholesterol dropped 9-15 percent and HDL cholesterol increased 4-7 percent. The LDL/HDL ratio was reduced by 12-21 percent. Amongst others, a study conducted by Bristol-Myers Squibb found that after 4-weeks' supplementation with gamma- and delta-tocotrienol (100 mg/

day), total cholesterol dropped by 15-22 percent, and LDL cholesterol decreased by 10-20 percent.⁹

Structural Differences

Knowing the difference between the molecular structure of tocopherols and tocotrienols is important to understanding why tocotrienols, but not tocopherols, can support healthy cholesterol levels. Tocotrienol and tocopherol molecules both have the same head, the site of their well-known antioxidant activities. However, tocotrienols and tocopherols differ in the molecule's tail. Tocotrienol has a shorter tail containing double bonds that reduce the activity of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, the enzyme controlling cholesterol synthesis and the same enzyme targeted by statin drugs. Tocopherols, on the other hand, have a longer structural tail without these double bonds and are therefore unable to reduce cholesterol.

Another key difference between tocopherols and tocotrienols has to do with the various isomers. Alpha, beta, gamma, and delta are among the isomers of tocotrienols as well as tocopherols. For tocotrienols, delta has the strongest cholesterol inhibition potency followed by gamma, alpha and beta. Only delta and gamma isomers found in tocotrienols are effective at lowering cholesterol due to the substitution and location of methyl groups at the head region of the molecule. Methyl groups are the simple addition of a carbon to 3 hydrogen molecules—CH₃. Tocotrienols with less methyl groups are called desmethyl tocotrienols and they are more active, tremendously affecting the health properties of this portion of vitamin E. Delta- and gamma-tocotrienols are desmethyl tocotrienols and are therefore the only two isomers that fit this cholesterol-reducing molecular formula. Tocopherols do not have the same advantageous molecular structure associated with lowering of cholesterol.

Mechanism of Action

Tocotrienols positively affect lipids in the body thanks to their ability to suppress the activity of HMG-CoA reductase.¹⁰⁻¹¹ Recently, it was reported that *only* gamma- and delta-tocotrienol stimulate the degradation of the HMG-CoA reductase.¹²

In addition, gamma- and delta-tocotrienol block processing of a certain protein

that helps control the LDL receptor and genes in charge of cholesterol-creating enzymes. This may influence triglyceride synthesis (or reduction) with importance in prediabetic and diabetic conditions. Other vitamin E forms (all four tocopherols and alpha- and beta-tocotrienol) do not degrade, downregulate, or block this cholesterol-controlling protein—only gamma- and delta-tocotrienol possesses this ability.¹²

Other Heart-Supporting Actions

Metabolic Syndrome and Triglycerides

An estimated 16 percent of people in the US, 47 million, have metabolic syndrome¹³ with defining hallmarks such as increased waist circumference, increased serum triglyceride levels, high blood pressure (hypertension), elevated serum glucose, and insulin resistance.¹⁴⁻¹⁵

Tocotrienols, especially gamma- and delta-tocotrienols, increase the heart's vascular and metabolic integrity, leading to improved management of metabolic syndrome. When blood sugar is high, it encourages the formation of advanced glycosylation end-products (AGEs). AGEs are formed when sugars react with proteins in the body, causing a process called cross-linking that is tied to premature aging. Cross-linking increases the stiffness of tissues, decreasing their function, such as during cataract formation, which is a classic example of cross-linking. Studies on rats in which diabetes was induced showed that gamma- and delta-tocotrienol prevented the increase of serum AGEs that occurred in animals not given tocotrienols. Administration of tocotrienols also resulted in a decrease in blood glucose and glycosylated hemoglobin (HbA1c).¹⁶ Lower HbA1c levels indicate better blood sugar control, whereas higher levels indicate how severely diabetes is progressing and the rate at which AGEs are being formed.

Tocotrienols have an effect on another metabolic syndrome component—high triglyceride levels. Rice bran oil containing tocotrienols lowered plasma triglyceride levels, LDL cholesterol, and hepatic triglyceride concentration, suppressing unbalanced lipid levels in diabetic rats.¹⁷

In several clinical studies with metabolic syndrome patients or diabetic patients, even small amounts of rice bran tocotrienols were shown to reduce symptoms. An aqueous extract of water soluble

TABLE 1. The Eight Stereoisomers of Vitamin E and Their Characteristics**TOCOPHEROLS (ALPHA-, BETA-, DELTA- AND GAMMA-TOCOPHEROL)**

- Alpha-tocopherol is the form most often found in vitamin E supplements.
- Tocopherols inhibit absorption of tocotrienols.
- Although they have strong antioxidant properties, tocopherols do not possess the ability to support healthy cholesterol levels.

TOCOTRIENOLS (ALPHA-, BETA-, DELTA-, AND GAMMA-TOCOTRIENOLS)

- Tocotrienols support healthy cholesterol and triglyceride levels, with delta-tocotrienol having the strongest effect.
- Tocotrienols, especially gamma- and delta-tocotrienols, increase the vascular and metabolic integrity of the heart and influence factors involved in the metabolic syndrome.
- Delta tocotrienols act as anticoagulants, reduce the size of atherosclerotic lesions and inhibit arterial plaque formation.

compounds from rice bran reduced hyperglycemia, glycosylated hemoglobin and insulin levels, while rice bran fiber reduced high lipid levels in both type 1 and type 2 diabetics.¹⁸ In another large clinical study, vitamin E intake from diet was associated with reduced type 2 diabetes risk.¹⁹ In type 2 diabetic patients, atherosclerosis progression is more rapid, and 80 percent of patients die of atherosclerotic events. In addition, LDL-lowering therapies normally prescribed for diabetic patients have many side effects, creating a need for alternative approaches. Tocotrienols, which have no known side effects, were shown to decrease serum total lipids by 23 percent, total cholesterol by 30 percent and LDL-cholesterol by 42 percent (from 179 mg/dL to 104 mg/dL) within 60 days in type 2 diabetics.²⁰ Supplementation of 75 mg/day delta-tocotrienol in a small open study was found to promote metabolic health, where triglyceride levels dropped 20-30 percent.²

Arterial Health

One of the first steps in atherosclerosis development is fatty streak formation in the arteries. This begins when circulating monocytes—white blood cells that are the first line of defense in the inflammatory process—adhere to the endothelium (cells that line the blood vessels). Although the monocytes are operating with the best intentions—they are trying to fight the inflammatory process—their adhesion to the cells of the artery walls reduces blood flow. Tocotrienols reduce expression of cellular adhesion molecules, preventing monocytes from tethering to the artery walls.²¹

Delta-tocotrienol showed the most profound inhibitory effect on monocyte cell adherence as compared to tocopherols and

other tocotrienol isomers.²² It has been suggested that this phenomenon occurs because delta-tocotrienol inhibits vascular cell adhesion molecules (VCAM-1), which play a key role in allowing monocytes to cling to the artery walls.²³

Another step in atherosclerosis development is the formation of unstable plaques, which occurs when platelets aggregate at the inner, inflamed surfaces of blood vessel walls, forming clots and eventually blocking arterial blood flow. In a human double-blind crossover study, delta-tocotrienol was significantly more potent in the inhibition of platelet aggregation than the other tocotrienol isomers, giving an overall inhibition of 71 percent, as compared to 5-37 percent with other tocotrienols.²⁴

Tocotrienols' effects on this inflammatory thickening of the walls of the larger arteries have also been compared in animals. Mice fed a diet designed to induce atherosclerosis were simultaneously given a diet rich in desmethyl tocotrienols. The mice receiving tocotrienols had a 60 percent lower plasma cholesterol level than the control group on the same diet without supplementation. Furthermore, atherosclerotic lesion size was reduced 10-fold in the tocotrienol group. Alpha-tocopherol, on the other hand, had no effect. This finding was further corroborated in a similar independent study where desmethyl tocotrienols inhibited atherosclerotic lesions in a mouse model of high cholesterol. Atherosclerotic lesion size in mice supplemented with desmethyl tocotrienols decreased 42 percent, whereas in the mice given alpha-tocopherol, mean lesion size decreased only 11 percent.²⁵ In another study, after tocotrienols supplementation, atherosclerotic lesion size in mice was 92-98 percent smaller than in the alpha-tocopherol and control groups.²⁶

The reason why desmethyl tocotrienols showed such promising effects is because, as previously mentioned, fully methylated tocotrienols and tocopherols do not have the cardiovascular benefits characteristic of desmethyl tocotrienols.²⁷

Another study of patients with carotid artery arteriosclerosis, the blocking of the artery supplying oxygen to the brain, showed that tocotrienols supplementation caused regression of carotid atherosclerosis over four years. In 88 percent of patients who took the tocotrienols, carotid artery stenosis regressed or stabilized. Of the placebo group, 60 percent deteriorated, and only 8 percent improved.²⁸⁻²⁹ Interestingly, total cholesterol decreased 14 percent and LDL cholesterol fell 21 percent in the tocotrienol group during the third and fourth year of the study.³⁰

Antioxidant Activities

Antioxidants play an important role in slowing atherosclerosis, especially by preventing LDL cholesterol oxidation, a process where fats essentially turn rancid in the body after being subjected to free radical damage (also known as lipid peroxidation). In a study evaluating the antioxidant efficiency of tocotrienols in inhibiting lipid peroxidation, reactive oxygen species (ROS) production, and other oxidation markers, delta-tocotrienol was found to have the greatest antioxidant properties among the tocotrienol isomers,³¹ due to the molecule being more easily incorporated into cell membranes.² A comparative *in vitro* study showed that a mixture of gamma- and delta-tocotrienol was 4-fold more efficient as scavenger of free radicals than other tocotrienol isomers.³²

Blood Pressure

Hypertension can also damage arterial walls, making them more susceptible to plaque formation. In recent animal studies, tocotrienols were shown to lower blood pressure. When hypertensive rats were given gamma-tocotrienol, an example of a desmethyl tocotrienol, for three months plasma and blood vessel lipid peroxides were reduced, and total antioxidant status was improved.³³ Gamma-tocotrienol reduced systolic blood pressure significantly, and improved nitric oxide synthase activity (NOS), both of which play a critical role in the pathogenesis of essential hypertension.³⁴ Tocotrienols' impact on hypertension was confirmed in humans, where tocotrienol-

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Fuoidan: Potent, New, Marine-Derived Immune Support

by Mitchell A. Fleisher, MD, DHT, DABFM, DcABCT

The ocean is a vast source of a large number of health-giving substances. Omega-3 fatty acids from deep sea fish are some of the best known of these marine-derived nutrients. However, a lesser known, but equally important sea-derived substance called fuoidan, a component of certain seaweeds, is beginning to emerge as a powerful tool for enhancing immunity and other important aspects of overall health and well-being. Furthermore, a purified extract of certified organic fuoidan harvested from the pristine waters off the coast of Nova Scotia provides health-supporting properties that are evident after consumption of even extremely low doses.

Scientists have conducted an extensive array of *in vitro* and animal studies that have found fuoidan exhibits powerful inhibitory action against herpes and HIV viruses. Furthermore, newer, human research is confirming what these *in vitro* and animal studies have found in the past. Other studies have delved into a number of immune-enhancing characteristics of fuoidan, indicating it may be of particular benefit for immune support during the cold and flu season.

Moreover, studies indicate fuoidan may improve cardiovascular health, reduce non-ulcer-related indigestion, control allergic reactions and even inhibit the prions (denuded, ancient, pre-viral DNA/RNA particles) responsible for the sheep version of “mad cow disease.”

What is Fuoidan?

Fuoidan is a sulfated polysaccharide found primarily in various species of brown seaweed, such as hijiki, kombu, limu, moui, mozuku and wakame. Variant forms of fuoidan have also been found in animal species, including the sea cucumber. Extensive pharmaceutical research has been performed with fuoidan, focusing on two distinct forms: F-fuoidan, which is composed of over 95 percent sulfated esters of fucose and U-fuoidan, which is approximately 20 percent glucuronic acid. As a result of this scientific research,

nutraceutical products containing purified concentrates of U-fuoidan and F-fuoidan are currently being made available as an immune enhancing food supplement.¹

Research regarding fuoidan commenced around 1970, and subsequently, fuoidan has been cited in approximately 700 studies published in the National Library of Medicine’s database. Overall, the findings of this substantial body of scientific research, together with anecdotal evidence provided by a long history of culturally-based use of fuoidan-rich seaweeds in regions such as Hawaii, Korea, Japan, Polynesia and Tonga, clearly indicate that fuoidan demonstrates great potential as a safe, nutritional support for a wide variety of health conditions.

Sea-Derived Immune Support

The most significant benefits of fuoidan pertain to its ability to strengthen the immune system. In a number of *in vitro* and animal studies, it has inhibited coated viruses such as herpes, HIV and human cytomegalovirus, a type of herpes virus that can cause blindness and fatal pneumonia in individuals with compromised immune systems. Experiments have suggested that fuoidan may not only inhibit the initial stages of viral infection, such as attachment to and penetration into host cells, but also the later replication stages after virus penetration.²

In another interesting study in mice, researchers tested fuoidan, along with a number of other agents, to see whether they could prevent genital herpes infections. The scientists administered fuoidan, or a number of other agents, to the vaginas of the animals approximately 20 seconds prior to inoculating the animals with a highly infectious herpes simplex virus type 2. The fuoidan was one of the agents that “provided significant protection” against herpes virus infection.³

A pilot study by University of Chicago researchers found similar properties when fuoidan was consumed orally by humans. Fifteen patients with active herpes-type

infections (including herpes simplex virus types 1 and 2, herpes zoster or Epstein bar virus) and six subjects with latent infections, consumed oral doses of fuoidan. Ingestion of fuoidan was associated with increased healing rates in patients with active infections. In addition, patients with latent infections remained asymptomatic while ingesting fuoidan.⁴

The ability of fuoidan to inhibit the herpes virus may explain, in part, why there is a much lower incidence of herpes simplex virus type 2 infections in Japan, compared with the west, in that the Japanese diet contains a high consumption of fuoidan-containing seaweed.

Researchers have also tested fuoidan against other sexually transmitted conditions, with promising results. Using a cell-line derived from the human cervix, researchers have shown that *Chlamydia trachomatis* infection can be blocked by fuoidan, which prevents the adherence of *chlamydiae* to target cells.⁵

The same researchers previously observed that fuoidan and similar substances could inhibit transmission of human immunodeficiency virus *in vitro*.⁵ They suggested that fuoidan and similar compounds “could be used in a vaginal formulation to inhibit infection by human immunodeficiency virus.” After conducting the follow-up study with the *chlamydia* pathogenic organism, the researchers noted, “The results of the present study suggest that the same type of formulation may inhibit sexual transmission of *chlamydia*.”⁵

In vitro studies testing fuoidan’s inhibitory effects on the HIV and herpes viruses have shown that fuoidan’s mechanism of action involves blocking virus entry into cells, rather than killing the virus directly. Fuoidan appears to specifically block the host cell surface receptor that the virus normally uses to enter the cell, rather than acting directly as a virus-destroying agent.⁶

Research that digs deeper into the mechanism of action of fuoidan indicates its reach extends far beyond simply inhibiting

viruses. It has been shown to influence the immune system in a number of ways. First, fucoidan has stimulated an increase in levels of a cytokine known as interferon gamma. Cytokines are proteins produced by white blood cells and are important in regulating immunity. Interferon gamma is a cytokine that generates increased immune activity during infections and cancer states.⁷⁻⁸

Another explanation for the immune-enhancing properties of fucoidan involve its ability to stimulate natural killer cells, which play an important part in the immune response by destroying cells infected with viruses. Natural killer cells are also vital to seeking out and destroying tumor cells and are a major defense against malignancies. In a recent study, researchers investigated the effects of fucoidan on the tumor growth of mouse leukemia cells and on T cell-mediated immune responses in mice. The animals were fed a diet containing 1 percent fucoidan for 10 days and subcutaneously inoculated with leukemia cells. Thereafter, the mice were fed with the diet containing fucoidan for 40 days. In mice receiving the fucoidan, tumors were inhibited by 65.4 percent. Additionally, natural killer cell activity significantly increased in the fucoidan-fed mice compared to animals fed a normal diet.⁹

A French research study in 2002 showed that F-fucoidan can inhibit hyperplasia (abnormal cell overgrowth) in rabbits.¹⁰ A Japanese research report in 2005 indicated that F-fucoidan can induce apoptosis (spontaneous, programmed, cancer cell death) in human lymphoma cell lines.¹¹

Clearly, the immune-enhancing properties of fucoidan have far reaching consequences for human health. Some studies are showing that it can down regulate the aspect of the immune system that is responsible for allergic reactions and help control allergic phenomena.

Fucoidan and the Heart

Fucoidan inhibits smooth muscle cell proliferation, which is of particular interest in arterial occlusions following placement of stents in heart patients.¹² This effect was confirmed in a study of rabbits given fucoidan by intramuscular and intravenous (IV) injection.¹³

A study using lamb hearts achieved similar results. The researchers induced cardiac ischemia (heart damage caused by oxygen

deprivation) in the hearts, then exposed a number of the lamb hearts to fucoidan. In the animal hearts exposed to fucoidan, there was better recovery of left ventricular function, coronary blood flow and myocardial oxygen consumption after ischemia.¹⁴

Fucoidan is thought to achieve these heart protective effects by blocking selectins, cell receptors important in the adhesion of white blood cells known as leukocytes to capillary walls. When leukocytes adhere to the blood vessel walls, it can lead to tissue damage, ultimately resulting in atherosclerosis (hardening of the arteries). Acting as a selectin blocker, fucoidan can inhibit the migration of leukocytes into blood vessel walls that occurs when oxygen is reintroduced into ischemic tissue (known as reperfusion ischemic necrosis) and thus prevent the organ damage that can occur after oxygen reintroduction.¹⁴

Fucoidan's role as a natural anti-coagulant (blood thinner) also may explain its protective effects on the heart, blood vessels and other vital organs.¹⁵

Thus, fucoidan has been demonstrated to possess significant cardioprotective activity that may be of particular benefit to anyone with cardiovascular health conditions and/or for prevention of heart and blood vessel problems.

Wide Variety of Applications

Fucoidan has been demonstrated to have a number of other interesting properties. In one clinical trial, subjects with non-ulcer dyspepsia (indigestion) were given 1.5 to 4.5 mg/kg/day of oral fucoidan for two weeks. Symptoms of non-ulcer dyspepsia were relieved in the subjects given fucoidan. Researchers believe these results are explained by studies that have shown fucoidan can stop the ulcer-causing bacterium *Helicobacter pylori* from adhering to gastric cells.¹⁶

Recently, fucoidan has been demonstrated to have inhibitory activity against the prion infection "scrapie."¹⁷ This disease is closely related to bovine spongiform encephalopathy (mad cow disease), but appears exclusively in sheep and goats. There is also evidence that fucoidan inhibits infection by the water borne parasite *Cryptosporidium*, which is responsible for serious, chronic infectious diarrhea, especially in immunocompromised persons, e.g., cancer and AIDS patients, etc.¹⁸

A Unique Form of Fucoidan

A special form of fucoidan is harvested in the pristine waters off the coast of Nova Scotia. It is extracted from organic-certified, hand-harvested seaweeds using a proprietary, solvent-free, coldwater process. Furthermore, the seaweed is collected just above the ocean's surface, not by dredging, thereby being an environmentally friendly, sea-farming process. This ensures that the seaweed is free from contamination and that the harvesting process produces minimal environmental impact while allowing the plant to continue to grow. This special method of extraction and the location of the ocean harvest ensures that the fucoidan is free from the heavy metal contamination that occurs in seaweeds produced in other areas of the world. This is particularly important as studies have shown that kelp supplements may be contaminated with arsenic.¹⁹

Conclusion

Fucoidan is emerging as one of the most intriguing immune system enhancers of our time, possessing strong inhibitory activity against a number of coated viruses, such as Herpes, Chicken pox (*Varicella*), EBV and HIV. Its ability to significantly enhance natural killer cell activity also indicates that it can strengthen immunity during the cold and flu season, as well as help protect against formation and growth of abnormal cells. Furthermore, the ability to help maintain cardiovascular and gastric health indicates that fucoidan may be one of the most important substances ever derived from the sea. Finally, it is essential that the most pristine and organic source of fucoidan be used as a nutritional supplement, otherwise the active constituents will not be present in the pure and sufficient quantities to be biologically beneficial.

**Mitchell A. Fleisher,
MD, DHt, DABFM, DcABCT**

Dr. Mitch Fleisher is the Chief Medical Board Advisor for CP.

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Childhood Weight Management: Helping Kids at an Early Age Essential for Long-Term Quality of Life

by Nieske Zabriskie, ND

The number of overweight or obese children in the U.S. is increasing at an alarming rate. The Center for Disease Control (CDC) has compiled data from two National Health and Nutrition Examination Surveys (NHANES) (1976–1980 and 2003–2004), which show disheartening statistics for the rate of increase of overweight children: for children aged 2–5 years, prevalence increased from 5.0 percent to 13.9 percent; for those aged 6–11 years, prevalence increased from 6.5 percent to 18.8 percent; and for those aged 12–19 years, prevalence increased from 5.0 percent to 17.4 percent.¹ These statistics are concerning since childhood obesity increases the risk of numerous chronic diseases, both as a child and as an adult, such as cardiovascular disease, diabetes and asthma. Furthermore, obesity has a negative impact on a child's self-esteem and self-worth, taking an emotional toll that is just as burdensome as the physical health consequences.

Health Consequences of Childhood Obesity

Asthma

Research indicates that there is an association between increased weight and asthma. One study showed that increased weight during middle childhood increased the risk of developing asthma by as much as 50 percent.² In fact, another study demonstrated that the lifetime prevalence for diagnosed asthma in normal weight girls is 3.5 percent, while the risk jumps to 10.3 percent for obese girls. No correlation in this study was found in boys.³

Cardiovascular Disease and Diabetes

A considerable amount of research exists regarding childhood obesity and the risk of cardiovascular disease and blood sugar disorders. One study examined the correlation between measures of adiposity such as body mass index, skinfold thickness, waist circumference, and waist-to-height

ratio and cardiovascular risk factors including plasma triglycerides, insulin levels, elevated blood pressure, and plasma high-density lipoprotein (HDL) cholesterol. This study showed that all measures of adiposity were associated with increased triglycerides, insulin levels and low HDL cholesterol. Also, it demonstrated that 7.7 percent of overweight children had at least 2 of these cardiovascular risk factors compared to only 0.25 percent of normal weight children. In fact, low levels of the beneficial HDL cholesterol were 20 times more frequent in overweight children than their normal weight counterparts.⁴

Additionally, researchers have examined the relationship between childhood obesity and vascular inflammation as a risk factor for the development of atherosclerosis. Researchers investigated levels of high-sensitivity C-reactive protein (hs-CRP) used to measure vascular inflammation in these children. They also looked for signs of early atherosclerosis including carotid intima-media wall thickness (IMT) used to measure sub-clinical atherosclerosis, and brachial flow-mediated dilation (FMD), a measure of blood flow. FMD is diminished in patients with atherosclerosis and with coronary risk factors, and improves with risk-reduction therapy. The study found that obese children had significantly elevated hs-CRP, increased IMT, and impaired FMD compared to controls suggesting early atherosclerotic changes.⁵ Furthermore, other researchers have investigated additional cardiovascular risk factors such as oxidant-antioxidant status, insulin resistance, as well as IMT. They showed that in obese children with a mean age of 8 years old, there is an increase in cardiovascular inflammatory markers, increased IMT, and increased fasting insulin and markers for insulin resistance.⁶ The American Diabetes Association states that 2 million adolescents aged 12–19—approximately 1 in 6 overweight adolescents—are pre-diabetic.

They also indicate that although national data does not exist regarding type 2 diabetes in children, regional studies show that type 2 diabetes is increasing in this younger population.⁷

Lifestyle Modifications

Poor eating habits contribute to childhood obesity. The strongest association remains between childhood obesity and the increased consumption of sugar-sweetened beverages. (See sidebar for a healthy alternative.) Additional research correlates being overweight in childhood with eating habits such as consuming less energy-providing foods at breakfast or more at dinner, skipping breakfast, buying lunch at school and eating dinner while watching television or without family supervision.⁸ Other researchers have shown that inadequate intake of fruits, vegetables and milk while consuming increased amounts of high-calorie snacks is associated with childhood obesity. More specifically, one Canadian study showed that in children over age 4, approximately 41 percent of daily snack calories comes from food such as soft drinks, fruit drinks, chips, chocolate bars, sugars, syrup, preserves, fats and oils. Low-nutritional value food intake was estimated at 22 percent of daily calories.⁹

According to the CDC 2005 survey, almost 80 percent of youth reported not eating the recommended 5 servings of fruits or vegetables per day in the previous week. This survey also showed that 67 percent did not attend any physical education classes.¹⁰ Additionally, the U.S. Department of Agriculture indicates that in youth ages 6–19, 67 percent exceed dietary guidelines recommendations for fat intake and 72 percent exceed recommendations for saturated fat intake.¹¹

Research indicates a strong relationship between childhood weight and level of physical activity. Increased physical activity

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CUSTOMER CORNER

Diabetes, High Cholesterol

Dear Dr. Dean,

I'm a prediabetic. My serum blood glucose is 112, total cholesterol is 214, triglycerides are 226, HDL is 39, VLDL is 45, LDL is 130. I want to try *Pressure-FX*[®], *GluControl*[™], *BHT*, and *Dilantin*. Is fixing my blood sugar the first thing to do? I also have herpes and gout. Since *Niacin* isn't good for gout, is there anything else I can take for my lipids?

Mr. R.

Dear Mr. R.,

I think your ideas are all good ones. Unless you've had problems with *Niacin*, you might give it a try. Although gout is a caution for taking *Niacin*, everyone is not equally sensitive to it and you may not have any problems. If you do, I recommend *Red Yeast Rice Extract*, along with *CoQ10-H₂*[™].

Ward Dean, MD

Hormone Balancing

Dear Dr. Dean,

My hormone panel results showed that my progesterone/estradiol ratio was low (10.0). In addition, my estradiol was 2.8 (high) and my cortisol noon 1.6, evening 1.1, night 0.3 (all low). I have low libido, poor sleep—otherwise all blood work good. I do not have much work stress, and I'm in great physical condition, although I may be over trained. What supplements should I take? *Pregnenolone*? Any help would be appreciated.

Mr. P.

Dear Mr. P.,

You didn't say how old you are. Also, it would be helpful to know your testosterone levels.

Having said that, I think your suggestion to add *Pregnenolone* is a good one, as that would help to raise your progesterone levels and balance your cortisol. You might also consider *BioDIM*[®] to help with estrogen excretion, and *Resveratrol* to prevent testosterone from aromatizing into estrogen.

Hope these suggestions help.

Ward Dean, MD

Anxiety Attacks

Dear Dr. Meletis,

My 81-year-old mother, who has been a customer for years, is having terrible anxiety attacks and is feeling nervous all of the time. She takes blood pressure medicine and *Armour*[®] thyroid medicine. She gets saliva tests done so that her hormones are in balance. She gets blood work done every six months for thyroid. As a matter of fact, she got results yesterday on her thyroid and was told it was fine.

Her health practitioner recommended that she take *GABA* and *Melatonin* (750 mcg). She was told to take *GABA* two times per day and *Melatonin* before bed. When she took the *GABA* in the morning the first day, she became VERY anxious and nervous—even more so than before. So she cannot do *GABA*. The *Melatonin* pill at night helps, but she still has anxiety attacks, especially at night. She sleeps 4 or 5 hours with the *Melatonin*. She lives alone; my dad passed away 5 years ago.

As I look in your catalog, I see a number of products, but I am not sure what would be best for her. I see the *Allay*[™], but it has *GABA* in it.

Please help!

Ms. T.

Dear Ms. T.,

I would suggest your mom continue working with her provider in regards to adding other items to her program. Clinically, I find it very helpful for my patients with anxiety to use *L-Theanine* in the morning, mid-day and evening. Additionally, increasing *Magnesium* intake can really help many patients. It is also critical to make sure your mom is sleeping well at night and not snoring; this can contribute to anxiety. Also *5-HTP* in the evening at bedtime can often help with anxiety throughout the day. I think the key is to figure out what is causing this anxiety; it is a clue that something needs fine tuning. Checking her blood pressure, getting an EKG and making sure electrolytes are balanced, is important.

Keeping her medical doctor informed, needless to say, also is very important.

Sincerely,
Chris D. Meletis, ND

Back Injury

Dear Dr. Dean,

Several years ago I injured my back. I had intense burning in the nerves. The burning also permeated my skin. I used numbing pads occasionally. My back got a little better. The burning slowed down. I twisted and it brought back severe burning, and once again it felt like it was in my skin also.

I went to a doctor in Fairfax, Virginia and he helped me a lot with prolotherapy. For about 8 months I was doing well. Now I have overdone it a little bit and the nerves are burning again. As before it feels as if it's in my skin. This has me so perplexed. It irritates me so badly when I drive because it's near my Sacroiliac joint. Even though there is no reaction seen on the skin, I cannot rub anything on that area and when I shower I have to block the area from water spray. Are there any nutrients that would help with this? I take proteolytic enzymes and thought about ordering your *Advanced Inflammation Control* product. Any suggestions would be appreciated.

Ms. E.

Dear Ms. E.,

The burning you are describing is classic nerve root pain, perhaps caused by a herniated disc or vertebral osteophyte.

I suggest a combination of *Nutri-Joint*, to help heal the disc, along with an "inversion device" (check this heading on the internet to see what I am talking about.) Use of the inversion device for 10-20 minutes per day should give you significant relief by taking the pressure off of the nerve root. Also, you might consider a TENS unit to provide some pain relief.

Finally, in addition to the proteolytic anti-inflammatory enzymes (*UniZyme*[™] is a good choice), you might try an anti-inflammatory supplement such as *Boswellia Extract*, or, as you suggested, *Advanced Inflammation Control*.

Hope these suggestions help.

Sincerely,
Ward Dean, MD

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CUSTOMER CORNER

Hashimoto's Thyroiditis

Dear Dr. Dean,

I have Hashimoto's Thyroiditis. Needle aspiration revealed two benign nodules. My thyroid stimulating immunoglobulin is 93, antithyroglobulin Ab 2508, thyroid peroxidase (TPO) Ab 582. These levels are extremely high and yet my physician says to wait.

I am a 57-year-old female with little energy, receding hairline and lots of weight gain. I am currently taking progesterone cream (*HerBalance™ Cream*) and Vagifem®. Will Inderal® help me? Thank you.

Ms. M.

Dear Ms. M.,

Usually, sufferers of Hashimoto's Thyroiditis experience symptoms of hypothyroidism (i.e. underactive thyroid). Inderal is prescribed for those with hyperthyroid symptoms, manifested by rapid heart rate. Inderal will normalize the heart rate and other symptoms of anxiety.

I suggest iodine replacement (as with *Iodoral®*). It might be a good idea to take our *Iodine Sufficiency Test* first, to help monitor your progress and iodine requirements.

In addition, I suggest anti-inflammatory substances such as *Advanced Inflammation Control*, *Turmeric Extract*, and/or *Boswellia Extract*.

Sincerely,
Ward Dean, MD

Oral Chelation, Extend Liquid

Dear Dr. Dean,

Our MD says he believes that chelation therapy works so we are considering *Oral ChelatoRx*. But are 12 per day excessive? If not, how long do you have to take it?

My second question is: If taking *Extend Liquid*, do we need to take a B-complex, vitamin C and zinc? We are trying to trim our expenses and don't want to duplicate unnecessarily.

Thank you.

Ms. B.

Dear Ms. B.,

Twelve capsules of *Oral ChelatoRx* provide 1 gram (1,000 mg) of EDTA, which is

a therapeutic dose. It is not excessive unless adverse effects are experienced. (The most common side effect is gastrointestinal upset or diarrhea, due to the amount of magnesium in *Oral ChelatoRx*, if taken with other magnesium-containing products). I usually recommend to start with 3-4 *Oral ChelatoRx* capsules per day, and gradually increase the dose until you find a dose that is just under bowel tolerance, up to a maximum of 12 per day. For those who are taking *Oral ChelatoRx* for preventive purposes, six capsules per day may be adequate.

I don't think you need to augment with B-Complex, vitamin C or zinc, although I do recommend that you consider *Essential Minerals* along with *Oral ChelatoRx*.

Ward Dean, MD

Crohn's Disease

Dear Dr. Meletis,

Are there any products to help with Crohn's disease? How long does it take to get relief? Thank you.

Ms. R.

Dear Ms. R.,

First, I must start by saying that working closely with your personal physician with a condition such as Crohn's is essential. So, please share the following educational material with your personal physician as you consider the approach you wish to pursue.

My patients with Crohn's invariably always test for food sensitivity to common foods consumed. It makes sense that foods that come in contact with the lining of ones colon can irritate and further inflame the tissues. A patient-ordered *Food Sensitivity Test* that offers insights as to individual reactions to 96 most common foods is available here.

In terms of GI health, probiotics such as *Culturelle®* can prove helpful. Additional *Glutamine*, an amino acid, is also popular to support GI health. Likewise, use of *Digestive Enzymes* with larger meals may help ease the digestive process. Once again, definitely a discussion worthy of input from your personal physician. Smaller meals, plenty of water, avoidance of chlorinated water and avoidance of nuts or foods that are tough to digest is important. No coffee, limiting red meat and focusing on easy-to-digest foods also is essential. In addition, I would strongly encourage you to read the articles

"Lectin Lock™ Natural Defense Against a Hidden Cause of Digestive Concerns and Weight Gain" and *"Lectins Their Damaging Role in Intestinal Health, Rheumatoid Arthritis and Weight Loss"* available on the website.

In terms of how long a natural medicine approach can take to assist your body, this varies based on your health, the severity of your condition, strictness of dietary changes, and stress in ones life, etc.

Sincerely,
Chris D. Meletis, ND

EpiCor®

Dear Dr. Meletis,

***EpiCor* is made from Brewer's Yeast. Is it a specific strain? I've noticed that I feel better if I take Brewer's Yeast. Is *EpiCor* better than Brewer's Yeast (*Saccharomyces Cerevisiae*)?**

Mr. P.

Dear Mr. P.,

Thanks for the very insightful question. *EpiCor* is a unique yeast ferment (S.C.). It has been demonstrated to have specific properties that far exceed any and all expectations for any known yeast derivatives. Whereas unfermented yeast could be compared to a beam of steel, *EpiCor* would be considered a skyscraper. It has an antioxidant power that continues even when diluted to one part per trillion. *EpiCor* actually leads to substantial increases in sIgA, the immune secretion that literally safeguards all our mucous membranes. Additionally, it upregulates the CD4 helper cell/CD8 suppressor cell ratio, making the immune system much more effective, enhances natural kill cell activity, increases calcium signaling (cell communication) and also possesses the ability to kill both *Candida Tropicalis* and other microbes.

Your question is excellent and it is great to see that you already have an appreciation for therapeutic yeast. *EpiCor* is certainly something you will enjoy learning more about. I encourage you to visit the free of charge Webinar offered by Dr. Alexander Schauss, available on the website.

Sincerely,
Chris D. Meletis, ND

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CUSTOMER CORNER

Excessive Sweating in 5-Year-Old

Dear Dr. Meletis,

My adopted 5-year-old son has a condition where he sweats from his palms and the bottom of his feet. Other than this, he is very healthy. Any recommendations? Your help would be greatly appreciated! Thanks.

Mr. P.

Dear Mr. P.,

Thanks for a great question. In clinical practice this condition presents on occasion. It would be helpful if you can find out if there is any genetic history of this condition for your son. Having some basic blood work done including thyroid (TSH and Free T4) at the very least, along with a chemistry panel and CBC with differential could offer potential insights. I find *Food Allergy Testing* can really help with many patients with this type of condition. The *Food Allergy Test* is offered here.

Additionally, fish oil (such as *Nordic Naturals DHA Junior Liquid*) and a daily multivitamin (such as *Kids Essentials*) can help create a healthy foundation. Also, observe whether his sweating is worse when hungry to see if there is a low blood sugar (hypoglycemia) component.

Sincerely,

Chris D. Meletis, ND

Aneurysm, Hemorrhage

Dear Dr. Meletis,

A friend of mine was recently diagnosed with having an aneurysm close to her heart. She also has lost her eyesight on one eye due to a hemorrhage and she has a leg condition (vascular problem) that makes walking painful. She is only 52 years old. Are *Ginkgo Biloba*, *Nattokinase* and EDTA (*Oral ChelatoRx*) safe for her condition? Any suggestions about what should be a must for her regarding supplementation?

Thank you very much for your time.

Mr. L.

Dear Mr. L.,

For anyone with a history of hemorrhage or an aneurysm, items that act as blood thinners such as *Ginkgo* and *Nattokinase* should actually be avoided. Of course, with

her complicated case at such a young age, she will want to check with her doctor prior to starting any supplements.

For my patients with these types of issues they will typically use *Glucosamine Sulfate*, *Chondroitin Sulfate*, *MSM*, *Vitamin C* and *Vein Support Formula*. The goal is to support the connective tissues of the body. The *Oral ChelatoRx* may be okay, yet without knowing the cause of the weak vessels, it requires careful consideration.

Additionally, find ways to control blood pressure so it stays on the low side of normal. *Pressure-FX®* is a popular item that can assist many people in this realm.

Ensuring the correct nutritional products are being taken can be a challenging venture. That is why many of my personal patients take an *Organic Acid Test* to better help identify their unique biochemical needs. The same *Organic Acid Test* that I use in my clinical practice is offered here.

The information above is intended as educational only, and is not intended as either diagnosis or treatment. Only ones personal physician is familiar enough with ones health to make specific recommendations.

Sincerely,

Chris D. Meletis, ND

Maintaining a Healthy pH Level

Dear Dr. Meletis,

Do amino acids need to be neutralized? Furthermore, are there other supplements we should be concerned about (such as *Niacin* to name just one) as well? How do we maintain proper urine pH when taking large doses of supplements? If *Calcium* or other antacids are recommended to keep urine pH at proper levels, how do we then properly supplement our *Magnesium* levels? Thank you for your help with this confusing issue.

Ms. E.

Dear Ms. E.,

Most supplements with rare exception actually help maintain a healthy pH. *Magnesium*, although the balancing agent for *Calcium* when it comes to muscle contractions, won't throw off pH as proposed. I personally recommend my patients use *NanoGreens¹⁰* in the AM and PM to help keep pH balanced. Its alkaline nature can be used to help ensure a nice buffering effect.

Additionally, keeping red meat and carbohydrates to a minimum and limiting stress will significantly offset acidic trending. In terms of *Niacin* and amino acids, with sufficient water intake these should not meaningfully change urine pH.

Many of my patients will fine tune their chemistry by taking an *Organic Acid Test/Metabolic Profile* along with a *Food Sensitivity Test* to help optimize their biochemical pathways and help control pro-acidic inflammatory responses. Both of these tests are available here.

Sincerely,

Chris D. Meletis, ND

SPECIAL WEBINAR

Tuesday, September 18, 2007, 12 pm EST.

Annatto Tocotrienol vs. Palm Tocotrienol – Discover the Difference

Learn why annatto is the best source of tocotrienol for your patients and about how it is a powerful cholesterol-lowering and heart-supporting properties not found in tocopherols during a live one-hour webinar presented by tocotrienol expert Barrie Tan, Ph.D., Tuesday, September 18, 2007, starting at Noon EST.

Dr. Tan earned his BS in Chemistry and Ph.D. in Analytical Chemistry at the University of Otago, New Zealand, and later became a professor at the University of Massachusetts Amherst teaching Chemistry and Food Science and Nutrition. His research expertise included lipid-soluble materials such as carotenoids, tocotrienols/tocopherols, CoQ10, omega 3s, and cholesterol. He was the first to introduce tocotrienol's benefits to our nutrition industry. He founded American River Nutrition, Inc. (www.AmericanRiverNutrition.com) in 1998 and developed the first ever tocopherol-free tocotrienol product from annatto beans.

To participate in this free webinar, please register at: <https://www.gotomeeting.com/register/658996160>.



Boron: Higher Doses Necessary for Cognitive, Bone and Joint Health

by Alexander G. Schauss, PhD, FACN

Boron is perhaps one of the least known and underappreciated minerals. Its bone- and joint-supporting abilities are often neglected in favor of calcium, when in reality it works with calcium to maintain healthy bones. Few individuals are aware of the other ways boron is important to health, including a surprising ability to enhance cognition. Because boron is so important to many aspects of health, it is particularly troubling that many individuals are deficient in this important mineral, increasing the risk of osteoporosis and arthritis.

Since 1923 boron has been recognized as an essential nutrient for plants. Among plants the deficiency of boron is the most common deficiency of any trace element.

Boron is not pervasive in the human diet. Instead it is found in significant amounts in only a few foods, leading off with apples (42.5 micrograms/gram of dry weight) and continuing down through soy meal (28 ug/g) then grapes, tomato, celery, almonds, broccoli, bananas, wines and honey (7.2 ug/g).

Today it is known that boron is present in body tissues and fluids found in the human body primarily as boric acid.¹ The Tolerable Upper Intake Level for boron set by the Food and Nutrition Board of the Institute of Medicine for boron has been established at 20 mg/day for adults over the age of 18 years.²

I first discussed boron, a little known trace element at the time, during the first national conference on nutrition and behavior held in 1982 at The University of Texas at Austin's LBJ Auditorium. I will never forget looking out over a confused audience of nearly 1,000 attendees as they glanced at each other and wondered why would anyone talk about a trace element for which there was no evidence of essentiality in any animal or in humans.

In the auditorium was Curtiss D. Hunt, PhD, a scientist studying trace elements at the US Department of Agriculture (USDA). He was surprised that anyone appreciated boron's potential role in human health and

had gathered enough data to keep an audience of nearly 1,000 scientists and health practitioners interested in the subject for more than half an hour.

Unlike 25 years ago, boron is now known to play a role in numerous metabolic processes affecting the health of animals and humans.³

Bone-Building Nutrient

Boron's role in human health is now known to be diverse. Inadequate boron intake is involved in inflammatory processes, including joint swelling, restricted movement, as well as body temperature, antibody production, blood hemostasis, serine protease (which is linked to platelet aggregation), activity of lipoxigenase (an enzyme that helps control inflammation) and metabolism of leukotrienes, chemical mediators of inflammation.⁴ However, perhaps boron's most well-known role in health is its ability to maintain the bones and joints.

In the audience at that 1982 conference was Forrest Nielsen, PhD, who at the time worked at the USDA's Grand Forks Human Nutrition Research Center in North Dakota. In subsequent years, Nielsen would demonstrate that boron deficiency combined with insufficient magnesium intake contributed to detrimental changes in bones due to suboptimal bone formation and maintenance.⁵ He and his colleagues demonstrated that inadequate boron intake depressed plasma ionized calcium and calcitonin and elevated plasma total calcium and urinary excretion of calcium. Today we know the mechanism of action better based on the discovery that boron deprivation in humans causes increased urinary calcium excretion.⁶

In addition to how suboptimal boron intake adversely affects bone health, boron and/or magnesium deprivation also causes changes that are seen in women with postmenopausal osteoporosis. This is because boron and magnesium are needed for optimal calcium metabolism. Without sufficient intake of both elements, bone loss is accelerated, which over time results in

excessive bone loss that can lead to osteoporosis in men and women.

Other research done with chickens demonstrated that boron supplementation stimulated the growth and partially corrected leg abnormalities in vitamin D3/cholecalciferol-deficient chicks.⁷ This suggested that one of the functions of boron appears to be its involvement in bone mineralization and structure. Years later it was shown that indeed this is true in pigs, whose metabolism and physiology is much closer to that of humans.⁸

When this discovery was factored into the incidence of osteoarthritis worldwide based on World Health Organization (WHO) statistics, it was discovered that people living in areas of the world with high levels of boron in the soil (and hence local foods) had a much lower incidence of arthritis, compared to those living in areas that had deficient levels. For example, the country with the highest arthritis incidence in the world, Jamaica, also had the lowest concentration of boron in the soil found in any country in the world.⁹

Part of the reason for this inverse relationship was more recently made clear with the discovery that dietary boron had a similar effect as supplementation with estrogen in humans.¹⁰ What is known today is that large amounts of dietary boron can benefit vitamin D3 and calcium status in humans.¹¹

Surprising Role in Hormonal Health

To understand this relationship between boron to calcium and vitamin D, some steroid chemistry must be explained. Boron is necessary for the formation of specific steroid hormones. A clinical trial has demonstrated that both 17-beta-estradiol and testosterone levels significantly increase in postmenopausal women consuming 3 mg/day of boron for 7 weeks.¹² In this study, boron supplementation caused a twofold increase in testosterone concentrations and a significant increase in calcium retention. In another study, men given 10 mg of boron a day for 4 weeks experienced a significant

increase in 17-beta-estradiol levels and an increase in plasma testosterone.¹³

Boron's ability to play a role in the formation of specific steroid hormones partially explains its effect on arthritis. Boron can complex with hydroxyl groups and form corticosteroids, which are known to alleviate symptoms associated with rheumatoid arthritis. Research performed in Australia demonstrated that when there were high levels of boron in the soil and water, the number of cases of musculoskeletal diseases was found to be 50 percent lower in areas that had low boron concentrations in water and soil.¹⁴

It is now believed that high levels of dietary boron can postpone the onset and lessen the severity of arthritis, which has already been demonstrated in experiments in rats, partially due to the inhibition of T-cell activity, associated with arthritis, and the modulation of serum antibody levels.¹⁵

Boron also has been shown to lower plasma lipid levels, possibly by decreasing lipid accumulation and promoting cholesterol removal for tissue although far more research needs to be done to explain how this works.¹⁶

Brain-Boosting Actions

Boron is much more than another mineral—it is a dynamic trace element when consumed in physiologic amounts that can affect a broad range of life processes involving macrominerals, energy substrates such as glucose and triglycerides, amino acids and proteins, free radicals and even estrogen. Any one of these processes cannot only effect the composition but also the function of numerous body systems.¹⁷

One of the most interesting aspects of boron's range of nutritional benefits is its positive effect on the brain and central nervous system. Inadequate boron intake can contribute to a lack of energy, ability to stay focused on tasks and mental alertness. To demonstrate this, I had a class of students taking a heavy load of second and third year med school courses participate as volunteers in a randomized, double-blind, placebo-controlled study, to help them gain practical experience in learning how clinical studies are designed.

The goal was to evaluate the effect of boron on mental alertness. Students received either a placebo capsule or 3 mg of boron daily for three months. Neither the

students nor I knew which student received the placebo and which student received the boron. After just one month I was fairly certain which students were taking boron supplements rather than the placebo based on my observation of their level of alertness and participation in class discussions. At the end of the study I discovered that I had correctly selected 92 percent of the students on boron based on my observations during class. When the code was broken and we found out whom had taken what, it supported not only their own impression as to whether they were on boron supplementation or placebo, but also mine as well. The difference was obvious to almost every student.

The explanation for these results was that inadequate boron intake lowered the activity in brain regions associated with alertness. This has been shown experimentally in humans who were carefully monitored for changes using an electroencephalogram (EEG) following boron supplementation.¹⁸

Widespread Deficiency

Many people ask: "Can't foods rich in boron meet my requirements for boron?" Unfortunately, the level of boron in a food depends on geographical factors, and worse, very few foods containing physiologically adequate levels of boron exist in the food supply chain to meet our needs. Even an apple, a good source of boron, can have very low levels of boron depending on whether it is grown in a dry or wet climate.

In early 1982 I was traveling from a nutrition conference in Australia to another nutrition conference in New Zealand. As luck would have it I found myself sitting next to a professor from Australia who was traveling to the same conference. I looked at the conference program and noticed he was going to discuss the role of trace elements in the development and treatment of arthritis in sheep. I found the title of his presentation quite puzzling as the conference was about human health, not sheep's.

What I quickly learned from him was that New Zealand had less than three and a half million people living in the country, yet it had over 65 million sheep. Hence, sheep were important to New Zealanders. What I also did not know was that sheep experienced the same kind of osteoarthritis that humans did.

What caught my attention was what he would discuss at the conference, and what I was privy to learn from his years of research: boron levels in the plants the sheep consumed determined the incidence and severity of arthritis. As a result of years of meticulous record keeping, he had observed a clear association between boron intake and osteoarthritis in sheep.

His research contributed to the growing evidence that certain rainy regions of New Zealand deficient in boron had much higher levels of arthritis not only in sheep but humans as well. It was in these areas of the country that the incidence of severe arthritis was dramatically high. By comparison, the driest parts of New Zealand, which experienced far less leaching of boron out of the soil, had much lower incidences of arthritis among sheep, with only the mildest symptoms associated with arthrosis (a joint disorder).

His astute observation led to a series of experiments. Sheep suffering from arthritis and grazing on land depleted of boron were given boron supplements. The animals showed marked improvements in mobility. In addition, the most surprising discovery was that the offspring had somehow acquired some protection from arthritis development later as adults when they continued to receive boron supplementation. Even more important was the recognition that this research might have implications in humans.¹⁹

Boron Supplementation

Because boron is rapidly absorbed and then excreted in the urine, its potential for toxicity in humans is of the lowest order. It has been reported that adults have tolerated 80 to 297 *grams* of boron.²⁰ However, in individuals with kidney problems, boron intake, like any intake of a mineral supplement, particularly potassium, should be carefully monitored as impaired kidney function could reduce excretion resulting in boron accumulation.

Conclusion

Boron is one of the most important minerals involved in bone and joint health. Its role is likely as important as calcium and vitamin D. Furthermore, boron can increase mental alertness, reduce inflammation and help in the metabolism of key hormones.

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Childhood Weight

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levels are associated with a lower BMI and less television watching. In fact, studies show that adolescents that participate in moderate physical activity more frequently have significantly decreased mean BMI. Those who reported increased vigorous physical activity had the lowest BMI compared to the other groups. Additionally, adolescents were 20-25 percent less likely to be overweight if they reported only 2-3 hours of television viewing per day and were 40 percent less likely to be overweight if they watched 1 hour or less compared to those who watch television 4 or more hours per day.¹²

Nutritional Support

The following nutritional strategies may be employed to help support weight management in children.

NanoGreens¹⁰. First and foremost, due to the inferior quality of most children's diets, finding a convenient way to provide them with the proper nutrients is essential. Fruit and vegetable drinks such as NanoGreens¹⁰ may be used to increase intake of phytonutrients that are often lacking in the diets of this high-risk population.

Xylitol. Xylitol is a naturally occurring sugar-alcohol that can be used as a low-glycemic dietary sugar substitute. Research indicates that compared to glucose ingestion, xylitol ingestion induced smaller changes in plasma glucose and insulin concentrations and did not induce reactive hypoglycemia.¹³ Xylitol also has dramatically reduced tooth decay¹⁴ and otitis media¹⁵ (ear infections), making it an ideal sugar substitute for kids with a sweet tooth.

Cinnamon. Cinnamon supplementation in healthy individuals has been shown to significantly delay gastric emptying and lower blood glucose levels after a meal.¹⁶ This effect is also seen in patients with type 2 diabetes. Research shows that cinnamon supplementation decreased fasting blood glucose levels by 18-29 percent and decreased cardiovascular disease risk factors such as triglycerides, LDL cholesterol and total cholesterol levels.¹⁷

Multivitamins. Multivitamins (such as Kids Essentials or Extend Core for older children who can swallow capsules) may

be indicated to support blood sugar metabolism and weight management. Numerous vitamins and minerals have shown to benefit blood sugar metabolism including chromium, magnesium, nicotinamide, vitamin E, vanadium, vitamin B6 and vitamin B12.¹⁸

Fish Oil. Fish oil is high in omega-3 fatty acids. Research shows that daily intake of fish and fish oils decrease the risk of glucose intolerance, a risk factor for type 2 diabetes.¹⁹ In fact, research also shows that a high intake of saturated fatty acids contributes to the risk of glucose intolerance and type 2 diabetes. Diets with increased intake of fish, potatoes, vegetables and legumes showed lower levels of blood glucose levels measured 2 hours after eating.²⁰ A good fish oil supplement for children is Nordic Naturals DHA Junior Liquid.

Conclusion

Overweight and obese children are increasing in number. The risk for chronic disease in this population is substantial. Parents, grandparents, family, care givers, pediatricians and individuals in the schools can greatly impact this growing health problem with multi-disciplinary interventions. Limiting television and video games, encouraging physical activity, and promoting diets high in fruits and vegetables and low in sugary snacks and beverages can benefit these children. Furthermore, substituting sugar with xylitol, ensuring a higher intake of essential nutrients through consumption of a green drink and children's multivitamins, and using fish oil supplements and cinnamon extract can help ensure that children maintain their optimal weight.

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Low Glycemic Smoothie for Kids

Studies show that eating a high-protein breakfast without blood-sugar raising carbohydrates can improve satiety and increase weight loss.¹⁻² Individuals who skip breakfast are more likely to feel hungrier later in the day, increasing cravings for foods that add pounds.

Sending a child to school nourished with a healthy meal can help maintain proper weight. To make sure your kids are getting a good and healthy start to the day, try this high-protein, antioxidant-loaded smoothie that won't raise a child's blood sugar to any appreciable degree.

Makes 1 serving

- 1 Cup Unsweetened Plain Low Fat Yogurt
- ½ Cup Frozen Berries (Or your choice of fruit that doesn't send blood sugar soaring such as apples or peaches)
- 1 Scoop of Smart Protein™ (Vanilla or Chocolate) or Rice Bran Protein Complex (for those with whey allergies)
- ½ to 1 Teaspoon Xylitol Crystals
- 1 Capsule Culturelle® Emptied into Blender
- ½ Teaspoon DHA Junior Liquid
- Strawberry Arctic Cod Liver Oil
- ½ Teaspoon Cinnamon
- 1 Tablespoon of Extend Liquid Multivitamin
- Natural Vanilla Extract to taste (Optional)
- Several ice cubes

Place all ingredients in a blender and blend until smooth.

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Resveratrol

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improved mitochondrial functions plus the activation of the Sirtuin family of longevity genes (see sidebar on pg 3). In addition to being a powerful antioxidant, trans-resveratrol acts like a molecular master key, "opening" or up regulating important genes and functionally related sequences of DNA or "families" of genes that directly control both the lifespan and metabolic efficiency. Trans-resveratrol also stimulates the production of ATP in the mitochondria of muscles.^{9, 15}

As a key regulatory molecule, trans-resveratrol improves cellular energy production and up regulates the expression of many different genes, leading to metabolic homeostasis as a prerequisite for a long and healthy life.

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Boron

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The widespread boron deficiency that exists throughout the United States and the world indicates that a higher magnitude of supplementation with this often overlooked mineral may positively affect many aspects of health.

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Tocotrienols

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rich vitamin E supplementation resulted in significant reductions in aortic systolic blood pressure and a 9.2 percent improvement in total antioxidant status.³⁵

Annatto: Unique Source of Tocotrienols

As mentioned previously, tocopherols do not have tocotrienols' cholesterol-lowering ability. In fact, alpha-tocopherol has been shown to attenuate or interfere with gamma- and delta-tocotrienols' cholesterol-lowering action.³ Therefore, it is important to find a supplement with a high tocotrienols content (especially gamma- and delta-tocotrienol) and a low tocopherols content. "Rice tocotrienols" contain about 50 percent tocotrienols and 50 percent tocopherols. "Palm tocotrienols" contain approximately 75 percent tocotrienols and 25 percent tocopherols. However, a little known tropical-rainforest-derived plant called Annatto ranks highest in tocotrienol content. Annatto contains 100 percent tocotrienols, and is virtually tocopherol-free. A special patented, solvent-free extraction of Annatto seeds produces the two most effective tocotrienol isomers: 90 percent delta-tocotrienol and 10 percent gamma-tocotrienol. Annatto is the only source of tocotrienols that contains 100 percent desmethyl tocotrienols and virtually no tocopherols.

Annatto-derived tocotrienols should be consumed 6 or more hours away from a multivitamin or other vitamin E supplement, due to the tocotrienol-inhibiting ability of tocopherols (the form used in most multivitamins and vitamin E supplements).

Conclusion

Tocotrienols possess powerful cholesterol-lowering and heart-supporting properties not exhibited by tocopherols.³⁶ Tocotrienols can help with premature aging associated with AGEs and support healthy cholesterol and blood pressure levels, arterial health, blood sugar regulation, and antioxidant protection. Gamma- and delta-tocotrienols have been found to be the most effective forms of vitamin E and are powerful antioxidants working at the cells' surface. Annatto is a particularly rich source of gamma- and delta-tocotrienols. It is virtually tocopherol free, indicating it is

a superior choice for a vitamin E supplement that produces documented support for the heart and entire vascular system.

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Vitamin C Improves Folic Acid Bioavailability

Researchers have found that consuming folic acid supplements with vitamin C may improve the body's ability to absorb folic acid. Researchers investigated the effect of simultaneous administration of a folic acid derivative on the folate status of nine healthy men. One group of men were given a placebo, another group the folic acid derivative only. Two other groups were given the folic acid derivative together with a low or a high dose of vitamin C.

Thirty minutes after administration, blood folate concentrations rose significantly compared to baseline measurements. However, in the two vitamin C groups, these elevated values lasted for six hours, compared to only four hours for the group receiving the folic acid derivative without vitamin C.

Reference:

Verlinde PHCJ, Oey I, Hendrickx ME, et al. L-ascorbic acid improves the serum folate response to an oral dose of [6S]-5-methyltetrahydrofolic acid in healthy men. *European Journal of Clinical Nutrition*. 11 July 2007. Epub ahead of print.

Bilberry and Black Currant Component May Possess Anti-inflammatory Properties

Increased consumption of the anthocyanins found in bilberries and black currants may prevent inflammation by affecting the activation of Nuclear factor-kappa beta (NF-kappaB), scientists have found.

NF-kappaB is activated by oxidative stress and pro-inflammatory stimuli and controls the expression of numerous genes involved in the inflammatory response. Dampening NF-kappaB activation and thereby limiting such a response have been suggested as a potential strategy to prevent chronic inflammatory diseases.

The researchers tested the effect of the bilberry and black-currant-derived anthocyanins on NF-kappaB response both *in vitro* and in a placebo-controlled clinical trial where the subjects were given 300 mg/day for 3 weeks. In the *in vitro* study, researchers exposed the cells to a substance that triggers an inflammatory response, then administered the anthocyanins. In the cells treated with anthocyanins, NF-

kappaB activation was reduced by 27.6 percent, compared to controls.

In the clinical trial, 120 subjects received the anthocyanin supplement or a placebo. Subjects given the anthocyanins from bilberry and black currants experienced a reduction in markers of inflammation. Interleukin-8 (IL-8) and interferon each decreased by 25 percent and T cell expression decreased by 15 percent, compared to the group receiving a placebo. In the subjects taking anthocyanins, researchers also noted a 60 percent drop in IL-4 and a 38 percent decrease in IL-13, two mediators of pro-inflammatory responses that can also trigger the activation of NF-kappaB. The placebo group experienced only a four and six percent decrease of IL-4 and IL-13, respectively.

According to the researchers, "These data suggest that anthocyanin supplementation may have a role in the prevention or treatment of chronic inflammatory diseases by inhibition of NF-kappaB transactivation and decreased plasma concentrations of pro-inflammatory chemokines, cytokines, and inflammatory mediators."

Reference:

Karlsen A, Retterstøl L, Laake P, Paur I, Kjølsvrud-Bøhn S, Sandvik L, Blomhoff R. Anthocyanins Inhibit Nuclear Factor- κ B Activation in Monocytes and Reduce Plasma Concentrations of Pro-Inflammatory Mediators in Healthy Adults. *J Nutr*. 2007 Aug;137(8):1951-4.

Mucins Help Strengthen the Intestines

Researchers have found that mucins, large proteins secreted on the surface of the gut, may act as a barrier to intestinal infections.

In the study, scientists orally infected mice with the bacterial pathogen *Campylobacter jejuni* (a common cause of diarrhea). One week after infection this organism could be detected in the organs of the vast majority of mice lacking mucin 1, but never in mice with intact mucin 1. Although *C. jejuni* entered the gastrointestinal epithelial cells that lined the intestines of both mice with and without the mucin 1, small intestinal damage as manifested by such factors as increased cell death (apoptosis) was more common in mice without mucin 1. The researchers concluded that the prevention of the spread of infection

was exclusively due to mucin 1 on the surface of gut epithelial cells.

The study authors wrote, "We believe this is the first *in vivo* experimental study to demonstrate that cell surface mucins are a critical component of mucosal defense and that the study provides the foundation for exploration of their contribution to epithelial infectious and inflammatory diseases."

Reference:

McAuley JL, Linden SK, Png WC, King RM, Pennington HL, Gendler SJ, Florin TH, Hill GR, Korolik V, McGuckin MA. MUC1 cell surface mucin is a critical element of the mucosal barrier to infection. *Journal of Clinical Investigation*. July 19, 2007. Epub Ahead of Print.

Mucins are found in Lectin Lock™, which contains a number of other substances to support intestinal health.

Vitamin D Deficiency Common in Adolescents Living in Northern Climates

Scientists have determined that as many as 55 percent of adolescents living in the Northeastern United States may be deficient in Vitamin D, increasing the children's vulnerability to such diseases as osteoporosis, cancer, and other health concerns later in life.

Researchers set out to determine the prevalence of and factors associated with low concentrations of 25(OH)D, a biomarker for vitamin D stores, in children and adolescents. The study authors measured serum 25(OH)D concentrations in 382 healthy children ages 6-21 years living in the Northeastern United States. The researchers conducted interviews to determine dietary and supplemental vitamin D intake. The researchers also determined factors associated with decreased concentrations of vitamin D.

The median concentration of 25(OH)D was 28 ng/mL, but 55 percent of subjects had 25(OH)D concentrations that fell into the deficiency category of less than 30 ng/mL.

Older age, black race, the winter season, and total daily vitamin D intake of less than 200 IU were some of the factors that influenced low vitamin D concentrations. In African-American adolescents, more than 90 percent of the children were deficient in vitamin D.



The results are particularly disturbing, given the role vitamin D plays in so many aspects of health, including building healthy bones. In fact, about 35 percent of a mature adult's peak bone mass is generated during puberty, indicating that a vitamin D deficiency during adolescence can have disastrous consequences later in life.

Reference:

Weng FL, Shults J, Leonard MB, Stallings VA, Zemel BS. Risk factors for low serum 25-hydroxyvitamin D concentrations in otherwise healthy children and adolescents. *Am J Clin Nutr.* 2007 Jul;86(1):150-8.

CoQ10 Improves Cardiovascular Function

A randomized, controlled clinical trial has found that oral supplementation with Coenzyme Q10 can improve blood flow and the function of antioxidant enzyme systems in patients with coronary artery disease.

The researchers randomly divided 38 coronary artery disease patients into two groups. One group of 19 subjects received CoQ10 orally at doses of 300 mg per day for 1 month, whereas the other group received a placebo. The researchers then studied whether the oral CoQ10 supplementation could improve endothelium-dependent vasodilation, the widening of the arteries to allow proper blood flow. They also studied CoQ10's effects on extracellular superoxide dismutase (ecSOD), a major antioxidant enzyme system of the vessel wall that is reduced in patients with coronary artery disease.

In the 33 patients who completed the study, levels of extracellular superoxide dismutase, the relaxation of the arteries and other improvements were significantly greater in the group taking CoQ10 than in the placebo group. In fact, the researchers noted that CoQ10-triggered improvements that "were remarkable" in subjects who had initially presented low initial endothelium-bound extracellular superoxide dismutase. This low level of ecSOD in patients prior to CoQ10 supplementation indicated the vessels were more prone to oxidative stress. The CoQ10-mediated increase in ecSOD indicated that oxidative stress in the vessels was reduced.

The researchers concluded that the results may be due to CoQ10's ability to

counteract nitric oxide oxidation as well as to its bioenergizing effects.

Reference:

Tiano L, Belardinelli R, Carnevali P, Principi F, Seddaiu G, Littarru GP. Effect of coenzyme Q10 administration on endothelial function and extracellular superoxide dismutase in patients with ischaemic heart disease: a double-blind, randomized controlled study. *European Heart Journal.* July 19, 2007 Epub Ahead of Print.

CoQ10-H₂[™] is a more bioavailable form of CoQ10 that can achieve similar effects at lower doses.

Tocotrienols Inhibit a Mutagenic Process Also Linked to Eye and Autoimmune Health

The form of vitamin E known as tocotrienols can stop angiogenesis, the development of new blood vessels that feed cancerous tumors, researchers have found in a new two-part study. The finding may also be relevant to rheumatoid arthritis and diabetic retinopathy, since both of these concerns also are linked to increased angiogenesis.

First, in an *in vitro* study, the researchers investigated which components of food might act as an anti-angiogenic compound in both bovine aortic endothelial cells and human umbilical vein endothelial cells. Endothelial cells are cells that line the walls of vessels. Through this testing, the scientists determined that tocotrienols could inhibit angiogenesis *in vitro*.

Then, the scientists undertook an *in vivo* mouse and chick egg study. They fed tocotrienols to tumor-implanted mice and noted the effect of the vitamin E component. Their findings indicated that angiogenesis in the animals that received tocotrienols was suppressed compared to the group that did not receive the tocotrienols. Mice given 10 mg of tocotrienol-rich oil per day (equivalent to 4.4 mg tocotrienols per day) experienced a 44 percent reduction in angiogenesis, compared to controls.

In the chick embryos, tocotrienols inhibited new blood vessel formation. At the same time, the tocotrienols also increased the area containing no blood vessels by 36 to 50 percent.

The researchers also conducted a separate third study to determine the mechanism of action behind tocotrienols' anti-angiogenic effects. This *in vitro* study showed that tocotrienols regulated growth of fibro-

blasts, cells that change cell signaling and induce programmed cell death (apoptosis) in endothelial cells.

Reference:

Nakagawa K, Shibata A, Yamashita S, Tsuzuki T, Kariya J, Oikawa S, Miyazawa T. In Vivo Angiogenesis Is Suppressed by Unsaturated Vitamin E, Tocotrienol. *J Nutr.* 2007 Aug;137(8):1938-1943.

Lactobacillus GG Supports Gastric Health

The probiotic *Lactobacillus rhamnosus* GG (also known as LGG or *Lactobacillus* GG) may accelerate the healing of gastric ulcers in animals, according to a new study.

Stomach or peptic ulcers result in a small hole in the gastrointestinal tract. Past research has found that the bacterium *Helicobacter pylori* is responsible for many stomach ulcers and that probiotics may inhibit *H. pylori*.

In the current study, scientists used acetic acid to induce ulcers in rats. The researchers then gave the animals *L. rhamnosus* GG intragastrically for three days.

The results indicated that the LGG successfully colonized the stomach lining, especially around the ulcer. LGG also significantly and dose-dependently reduced gastric ulcer area. LGG also decreased cell death, increased cell proliferation, and encouraged angiogenesis, the formation of new blood cells.

LGG's mechanism of action appeared to be its ability to influence protein expression in the stomach wall cells. This leads to increased formation of new blood cells and increased healing of the ulcer. The LGG did not produce changes in the animals with a healthy gastric tract, indicating LGG does not affect the function of normal gastric mucosa, but rather normalizes gastric function in individuals with abnormal gastric mucosa.

Reference:

Lam EK, Yu L, Wong HP, Wu WK, Shin VY, Tai EK, So WH, Woo PC, Cho CH. Probiotic *Lactobacillus rhamnosus* GG enhances gastric ulcer healing in rats. *Eur J Pharmacol.* 2007 Jun 22;565(1-3):171-9.

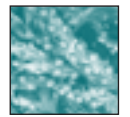
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Childhood Weight Management:

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