In This Issue

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Focus

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Ecklonia Cava Extract: Superior Polyphenol Antioxidant
Many Times Stronger Than EGCG

Ecklonia Cava Extract (ECE) is a standardized natural complex of unique marine molecules that originate from a specific species of brown algae (*Ecklonia cava).* ECE represents a unique category of polyphenols often called phlorotannins. ECE is considered a "super antioxidant" as it has up to eight interconnected rings, making its free-radical scavenging ability 10-100 times more powerful than other polyphenols, including green tea catechins. Dr. Haengwoo Lee and his team of M.D.'s and Ph.D.'s have spent over thirty million dollars on research, from *in vitro* to animal and human studies. ECE has been found to be an impressive therapeutic agent in a wide array of clinical applications including memory enhancement, relaxation, alertness, arthritis, inflammation, neuralgia, fibromyalgia, allergies, asthma, coronary artery disease, hypertension, ACE inhibition, high cholesterol, diabetes, erectile dysfunction, weight loss and obesity.

Turn to page 2 for more on ECE.

Traditional Vietnamese Herb *Crinum Latifolium* Shows Promise for Prostate & Ovarian Health

Crinum latifolium shows promise to become one of the leading treatments in the world for benign prostate hypertrophy (BPH) and ovarian conditions, including polycystic ovarian syndrome. Its benefits for prostate cancer should be explored.

"I have found Crinum to be universally effective for several patients with ovarian cysts."
– Dr. Abram Ber, M.D.

Turn to page 8 for more on Crinum latifolium.

The Strange Case of Strontium
A Reason Based Editorial

Osteoporosis is not caused by a strontium deficiency, so why the commotion over this trace mineral? By examining what high-dose strontium actually does to bones, and identifying a key element that is overlooked in the commentary about strontium, we can suggest a better model for the use of nutritional strontium.

Turn to page 11 for more on Strontium.

Ecklonia Cava Extract Super Antioxidant & Beyond

Ecklonia Cava Extract: Polyphenol / Phlorotannin Derived from Brown Algae

Ecklonia Cava Extract (ECE) is a standardized natural complex of unique marine molecules that originate from a specific species of brown algae (*Ecklonia cava).* ECE represents a unique category of polyphenols often called phlorotannins. Their unique polyphenolic structure endows them with biological activities that are not found in land-based plants.

ECE naturally occurs as high-molecular weight tannin (Mw> 2,000 Dalton) and low-molecular weight tannin (Mw=400-1000 Dalton). ECE can be classified into four types depending on the ratio of high molecular weight and low molecular weight tannins. Various physiological activities of ECE have been evaluated *in vitro*, *in vivo* and clinically as individual compounds (ECE1-ECE14) and complex forms (ECE, Type I-IV).

Millions on Research

Dr. Haengwoo Lee and his team of M.D.'s and Ph.D.'s have spent over thirty million dollars on research, from *in vitro* to animal and human studies. Much of the work was done in Korea, and some at the University of Washington. ECE has been found to be an impressive therapeutic agent in a wide array of clinical applications.

SUPER ANTIOXIDANT

The power of an antioxidant is determined by its structure, which is made up of rings. These rings capture stray electrons from free radicals. Most flavonoids generally have three interconnected rings. ECE has up to eight interconnected rings, making its free-radical scavenging ability 10-100 times more powerful than other polyphenols. It is substantially more powerful than green tea catechins, which only have four rings.

Multiple Antioxidant Profiles of ECE

ECE's antioxidant activities against various reactive oxygen species have been confirmed to be highly potent in physiologically relevant concentrations. The effective dose of ECE for free radical scavenging is in the 10-20 µg/mL range which belongs to most potent families of natural antioxidants. ECE itself and its individual compounds have demonstrated potent reducing power and radical scavenging activities against DPPH radical, oxidized LDL and peroxynitrite.*

Much Longer Half-Life

ECE is a unique polyphenol in that it has a very long half-life in the body. This is because ECE is a marine-based polyphenol which is 40% fat-soluble. Virtually all other polyphenols are derived from land-based plants and are water-soluble. The half-life of ECE is up to 12 hours, compared to 30 minutes for water-soluble, land-based polyphenols. ECE has the ability to cross the blood-brain barrier.

The Research of Martin Pall, Ph.D.

Peroxynitrite is the most notorious of the free radicals incriminated by Martin Pall, Ph.D.'s groundbreaking research on multiple chemical sensitivity, fibromyalgia, chronic fatigue syndrome, post traumatic stress disorder, Gulf War syndrome, and fourteen other conditions. Peroxynitrite plays a main role in Dr. Pall's mechanism, along with NF-kappaB and other inflammatory mediators. ECE also reduces tissue specific NF-kappaB.

FIBROMYALGIA

ECE: Phase I Clinical Trial Results (Preliminary)

In an 8-week, double-blinded, placebo-controlled study of established fibromyalgia patients, ECE was used as an adjunct therapy to the patients' current standard of physician care. The results established the general safety of ECE. ECE cut the time it took the participants to fall asleep by 47 minutes; it increased total nighttime sleep by 1.6 hours; it improved soundness of sleep by 80%; it boosted their energy levels by 71%; it gave them 2 1/4 more good days per week; it helped reduce their pain by 31%; and their general condition improved by 39%. Interestingly, these improvements were achieved at all doses. Patients given the placebo had no improvement during the study. *(See graphs opposite page)*

BRAIN FUNCTION: MEMORY, RELAXATION, ALERTNESS

Acetylcholine & Memory

Memory is dependent on the neurotransmitter acetylcholine (ACh). In an animal study, ECE increased rodent ACh by 140% in brain regions responsible for learning and memory in seven days. Memory enhancement increased by 100-200% at an oral dose as low as 0.2-1mg/kg.

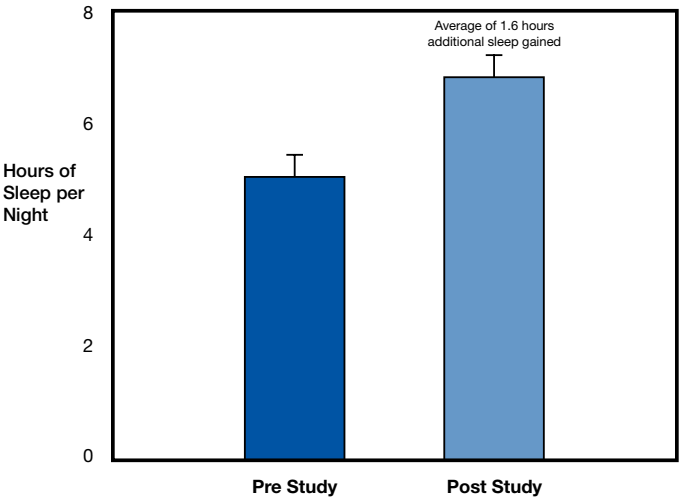
With regard to mechanism, it is thought that the mild acetylcholinesterase inhibitory activity of two phlorotannin compounds found in ECE, dieckol (DE) and phlorofurofucoeckol (PFF),

*Peroxynitrate is a central reactive oxidant, which appears to play a major role in many disease processes.

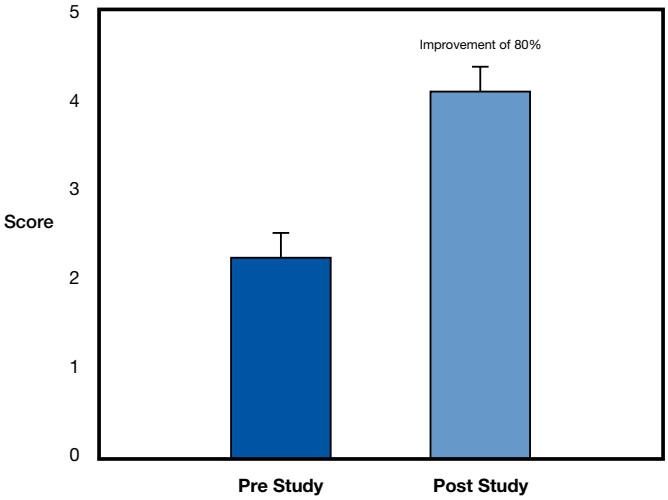
Continued on page 4

ECE & FIBROMYALGIA

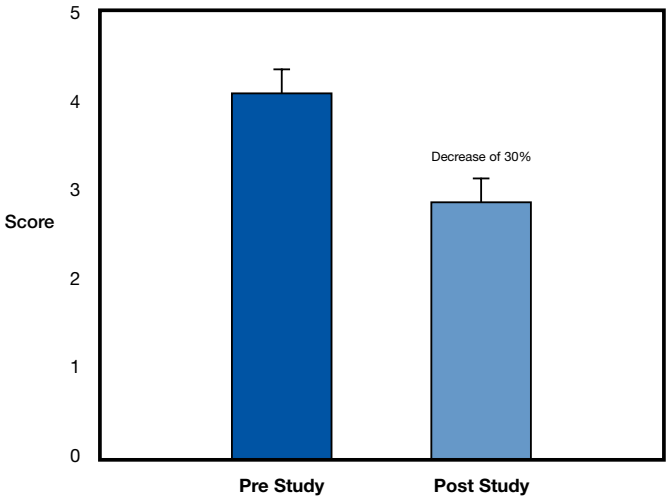
Affects of Hours Slept Each Night Before and After ECE Therapy p<0.001



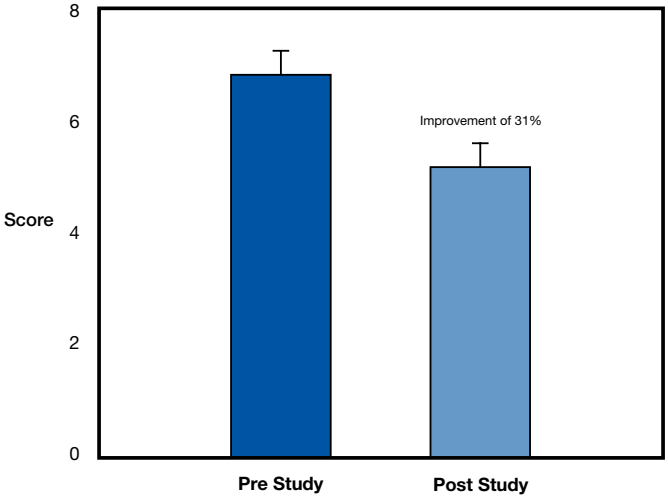
ECE Treatment Improved the Quality of Sleep and Ease of Falling Asleep p<0.001



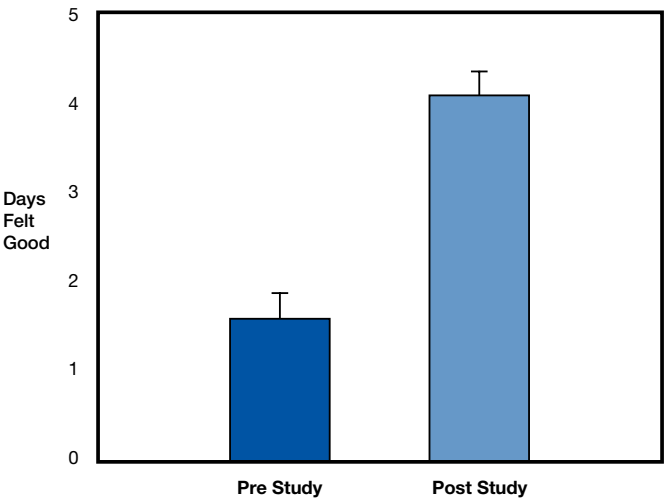
Overall Fatigue Levels Declined 30% after ECE Therapy - p<0.001



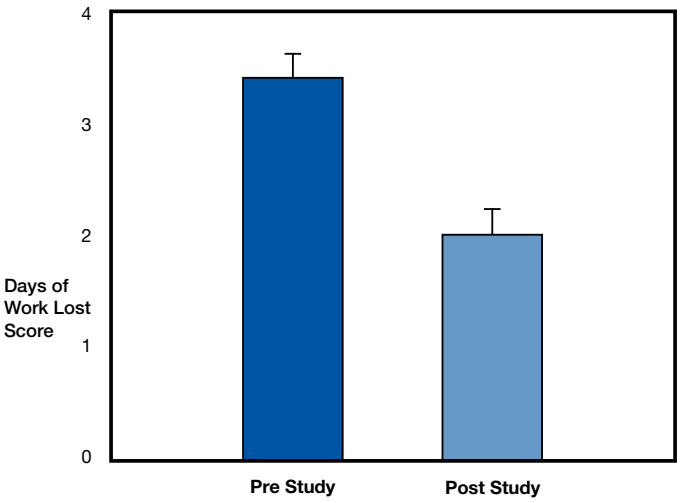
Summary Data for Pain Inventory p<0.001



ECE Therapy Improved the Number of Days per Week Felt Good by 56 hours p<0.001



ECE Therapy Reduced Lost Time at Work by 40% p<0.001



may be involved in the up-regulation of acetylcholine.

Increased Blood Flow

ECE crosses the blood-brain barrier and significantly improves blood flow, which is likely another way ECE improves memory. More specifically, Dr. Lee's group found that ECE can increase the velocity of blood flow in the carotid artery from an average of 36.68 cm/sec. to 40.09 cm/sec., while the placebo showed no improvement.

Relaxation & Alpha-Waves

An EEG study on brain waves of healthy middle age volunteers found that ECE compounds increase alpha-waves. Alpha-waves are an indicator of relaxation.

Alertness

Yet another study found that ECE compounds prevented sleepiness in bus drivers and in high school students during daytime activities. This is likely due to increased blood flow and oxygen delivery.

Neuroprotective Effects

ECE demonstrated powerful neuroprotective effects owing to several features of its components. ECE compounds are both powerful antioxidants and anti-inflammatory agents capable of scavenging free radicals and suppressing excessive inflammatory reactions. Fucoidan in ECE has recently been found to protect neuronal cells from ischemia-induced inflammatory reactions which often occur in the aged and highly stressed brain. ECE compounds also neutralize the neurotoxic free-radical peroxynitrite.

Enhancement of Acetylcholine Levels in Mice

After 7 days oral administration of two ECE compounds (DE 10mg/kg and PFF 2mg/kg), mice under ethanol-induced cognitive impairment showed substantial enhancement of acetylcholine in three brain regions related to memory formation, as compared with non-treated mice. Especially, 140% enhancement was observed in the frontal cortex that is crucial in long-term memory and associative thinking.

Resistance of Stress-Induced Learning Deficit in Mice

In a 5-day study, ECE treated mice showed significant resistance to electric shock treatment-induced learning deficiency, as compared to non-treated mice whose learning process was significantly retarded during the test period.

Memory Enhancement in Mice

The beneficial effects of ECE compounds on memory enhancement were further demonstrated by measuring the latency time avoiding the previously experienced electric shock treatment in mice as passive-avoidance memory testing. After 7 days oral administration of two ECE compounds DE and PFF (as low as 1 and 0.2mg/kg), mice under ethanol-induced cognitive impairment showed 130-140% improvement, especially in the PFF group.

Beta-Amyloid Deposition Inhibition in Rats

Researchers at the National Institute of Health's aging research labs in Baltimore studied ECE in rats, and found it to inhibit beta-amyloid deposition in the brain. Beta-amyloid is the same substance that accumulates in Alzheimer's disease. The rats also learned maze challenges faster, which demonstrated improvement in short-term memory.

ARTHRITIS INFLAMMATION NEURALGIA

Dr. Lee and colleagues found ECE to naturally suppress inflammatory responses and neutralize inflammatory damage caused by reactive oxygen species. The optimal combination of ECE's natural anti-inflammatory and tissue-protective properties appears to enable dramatic improvement in both arthritis and neuralgia. In a human trial, ECE significantly reduced pain in a group of knee arthritis patients compared with placebo.

Comparable to Celebrex®

ECE's ability to treat arthritis was found to be comparable to Celebrex®, the prescription drug that reduces inflammatory cox enzymes.

The influence of ECE in lipopolysaccharide (LPS)-induced generation of prostaglandin E2 (PGE2) using RAW 246.7 cells was studied. While PGE2 was barely detectable in non-stimulated cells, more than one hundred times the amount of PGE2 was detected in the stimulated cells. ECE, celecoxib (Celebrex®) and aspirin all showed significant inhibition of PGE2 generation in the concentration range tested. ECE showed inhibition of 61%, 85%, 92% and 99% at concentrations of 10, 30, 60 and 100 µg/mL, showing similar activity to celecoxib which showed 65%, 79%, 85% and 96%.

Cartilage Protecting Activities

As demonstrated above, ECE compared almost identically to celecoxib in the ability to reduce PGE2 by slowing down the lipoxygenase (LOX) system. ECE compounds have more than double the ability of resveratrol to inhibit LOX. These results were demonstrated in a study on rabbit cartilage cells. Those cells treated with ECE had up to an 80% reduction in degeneration.

Rabbit Model

In an animal study, rabbit articular cartilage explant culture was treated with recombinant human interleukin 1 (rhIL-1) to induce proteoglycan degradation. The amount of glycosaminoglycan released into the medium was measured as an index of proteoglycan degradation. When the rabbit cartilage explants were treated with rhIL-1 for 60 hours, the amount of released glycosaminoglycan into the culture medium

increased significantly compared to the vehicle group (1.44 ± 0.06µg/mg vs. 0.30 ± 0.01µg/mg). Diclofenac, which is known as a selective COX-2 inhibitor was used as a positive control at a dose of 10µM (3.2µg/mL). ECE significantly interfered with the rhIL-1-mediated degradation of proteoglycan in all concentrations tested ($p < 0.001$). It showed 53%, 79%, 81% and 70% of inhibition at 1, 3, 10 and 30 µg/mL concentration.

Neuropathy: 4-Week Clinical Trial

Researchers recently studied ECE on 40 patients with neuropathy. ECE reduced nerve pain by 40% in four weeks. Overall, 80% of the patients responded favorably.

Speculation about Neuropathy Mechanism

The strong lipid and cholesterol reducing potential of ECE supports reduced vascular inflammation. Increasingly, the scientific literature supports the notion that many forms of nerve pain or neuropathy are caused by nerve pressure, as exerted by swollen, inflamed blood vessels adjacent to the nerves.

ALLERGIES / ASTHMA

Overall, ECE appears to significantly relieve allergic reactions without drowsiness, dizziness and other side effects of anti-histamine drugs.

Allergic Inflammation: Mouse Model

Dr. Lee and his team found that ECE significantly reduced allergic inflammation in mice. Specifically, ECE reduced the migration of eosinophils to the lungs by 75%. Inflammatory white blood cells (CD4+4 T Cells, resultant cytokines Il-4, 5, 13) were reduced by 50%. Mucus plugs in the airways were reduced by 75%. Airway epithelial hyperplasia reduced by 75%. Collagen-causing fibrosis in lung interstitium (fibrosis, airway remodeling) and smooth muscle cell thickness was reduced by 20% and 32%. These latter findings suggest that ECE compounds can prevent or reverse the progression of chronic lung disease such as asthma and Chronic Obstructive Pulmonary Disease (COPD).

5-Lipoxygenase (5-LOX)

5-Lipoxygenase (5-LOX) catalyzes the first step in the oxygenation of arachidonic acid, thus leading to the production of biologically active compounds such as leukotrienes and 5-hydroxyeicosatetraenoic acid. The peptidoleukotrienes (leukotriene C4, leukotriene D4 and leukotriene E4) are powerful spasmogens, which have been implicated in inflammatory and allergic responses. Therefore, inhibition of 5-LOX is a medicinal target for the treatment of inflammatory diseases. One of the ECE compounds (8,8-BE) significantly inhibits 5-LOX compared with other well-known natural medicinal compounds such as resveratrol and EGCG.

University of Washington Asthma Mouse Model

The efficacy of ECE for asthma was demonstrated in an allergen-induced murine asthma mouse model by Dr. Emil Chi, Chairman, Department of Histopathology, University of Washington.

The researchers tested an ECE product (KLS) in a mouse model of allergen-induced chronic lung inflammation and fibrosis. BALB/c mice, after intraperitoneal antigen sensitization on day 0 and day 14, were given weekly intranasal inhalations of antigen from day 14-60. The antigen-treated and challenged mice developed an extensive eosinophil and mononuclear cell inflammatory response, mucus cell hyperplasia and mucus occlusion of the airway.

KLS was found to be effective in reducing allergic reaction in inflammation. By feeding at a concentration of 5.4 mg/ml in the drinking water for 12 days, KLS reduced the airway mucus plugging, and sub-epithelial fibrosis in the antigen-sensitized / challenged mice. The reduced BAL fluid eosinophil indicated that KLS is effective in improving the asthmatic lung structures. No pathological alterations in the liver, kidney, spleen, or small intestine were found.

CARDIOVASCULAR BENEFITS

Coronary Artery Disease

ECE has been shown to improve coronary artery disease (CAD). Researchers found that ECE is even more potent at inhibiting the oxidation of LDL cholesterol than green tea catechins, and appears to scrub the plaque off the endothelial lining. ECE also reduces vascular inflammation by preventing oxidation, which also directly effects inflammatory mediators such as inflammatory prostaglandins, etc.

Coronary Artery Disease: 6-Week Clinical Trial

A clinical trial using ECE was conducted confirming its capacity to regenerate vascular endothelium and recover plasticity of blood vessels after 6 weeks of treatment by measuring flow-mediated dilation (FMD) & nitroglycerin-mediated dilation (NMD) of normal and CAD patients with narrowed coronary arteries by 50+%. FMD indicates nitric oxide (NO) releasing ability of endothelial cells to expand blood vessels by detecting shear stress caused by incoming blood flow (low FMD value can indicate endothelium damage).

After 6 weeks of treatment with ECE, clinical data showed that FMD, the endothelium-dependent dilation, was greatly enhanced in the CAD group, indicating its remarkable activity of inducing recovery of endothelial cells. NMD, the endothelium-independent dilation, which represents the vascular plasticity, also showed remarkable improvement in the CAD group, again supporting ECE's ability to support restoration of vascular integrity by reversing atherosclerosis.

Continued next page

Cholesterol: 6-Week Clinical Trial

Researchers gave 39 adults (average age 55.6) low dose (100 mg) ECE compounds for six weeks. Their average cholesterol dropped from 228 to 224. LDL dropped from 141 to 135. HDL rose from 46.5 to 50.7 (highly significant). Triglycerides fell from 215 to 195, and the atherogenic index dropped 12.5%.

Some of the parameters from the above study show very mild changes, which in themselves, may not be statistically significant. However, all parameters went in a health-positive direction, so taken together, the changes in LDL, HDL, triglycerides, blood pressure, and antioxidant protection are very significant. Also, endothelial cells were protected against oxidative damage, and were able to produce significantly more NO, which dilates blood vessels. Dramatic increases in blood flow were also found at this low dose.

Hypertension: 4-Week Animal Study

The remarkable effect of ECE on vasodilation was clearly demonstrated in renovascular clipping induced hypertensive rats. Renovascular clipping surgery is known to increase ACE activity via the renin-angiotensin-aldosterone system, which increased systolic blood pressure (SBP) from 140 to over 200 mm Hg after 4 weeks. Upon oral administration of phlorotannin (99.4%, 50 mg/kg) or enalapril (commercial hypotensive drug, 10 mg/kg) SBP dropped to as low as 160 and 140 mm Hg. Upon cessation of treatment, SBP increased again in both cases. Although ECE showed a similar pattern to the drugs, it also showed a slower rebounding of blood pressure during the no treatment period, which indicates its potential as a vascular protector with prolonged oral administration.

ACE Inhibition

Angiotensin-converting enzyme (ACE), is responsible for conversion of angiotensin I to angiotensin II and degradation of bradykinin, and is a key component in the renin-angiotensin-aldosterone system. Angiotensin II regulates cellular proliferation, inflammation, and endothelial function, and is therefore important in the pathogenesis of atherosclerosis and its complications. Aging or various vascular risk factors tend to increase ACE levels resulting in excessive vasoconstriction and hypertension. Current hypotensive drugs block the action of ACE or its by-product angiotensin II.

ECE tannins have been found to be potent natural ACE inhibitors, demonstrating more than 15 times the power to inhibit ACE as the most powerful land-based polyphenols, including the natural hypotensive substance catechin found in green tea. One of the compounds found in ECE, THP-BE is comparable to the physiological vasodilative hormone bradykinin.

Antiplasmin Inhibition

Plasmin (a fibrinolytic enzyme that breaks down blood clots) is rapidly blocked by a protein called antiplasmin. ECE compounds are natural potent inhibitors of anti-plasmin, capable of efficient promotion of plasmin that performs fibrinolysis. ECE compounds have shown remarkable activity which is 40-200 times greater than synthetic compounds Flufenamate and Chloramine T. One study on ECE compounds found a small but significant rise in prothrombin time and a fall in fibrinogen levels.

ERECTILE FUNCTION ECE V. VIAGRA®

Nitric Oxide

ECE can regenerate the vascular endothelium, the cells critical to the inner lining of the blood vessels. They generate the chemical nitric oxide (NO), which keeps the arterial walls relaxed and dilated. After a six-week study of ECE, flow mediated dilation and NO mediated dilation increased by 60% and 50%. In another study, coronary artery disease patients were given ECE for six weeks. Blood flow controlled by NO increased 50-60%. These results confirm that ECE can rejuvenate damaged endothelial cells to produce NO. This effect was further confirmed in a study on erectile dysfunction (see below). Interestingly, Viagra® works by increasing NO in the penile artery.

ECE v. Viagra®: 8-Week Clinical Trial

Scientists studied 31 men with erectile dysfunction (ED) for over six months. They compared eight weeks of ECE use to Viagra®. They looked at orgasmic function (OF), intercourse satisfaction (IS), overall satisfaction (OS), and erectile function (EF). Over those eight weeks, ECE scored 87%, 74%, 62%, and 66%. Viagra® scored 27%, 44%, 39%, and 66%. No side effects were reported with ECE:

Population with 25+% Improvement in IIEF (International Index of Erectile Function) score was as high as 81%. Total IIEF score significantly increased from 29.1 ± 13.1 to 47.0 ± 14.5 with 62% of improvement. When the IIEF scores were grouped into five separate domains, mean IIEF scores at the 8th week were significantly greater than those at week 0 for all domains (all $p<0.01$). The degree of improvement was significant in the following order: OF (87%), IS (74%), EF (66%), and OS (62%). Scores on key questions (asking frequency of penetration and asking frequency of maintaining an erection after penetration), which directly indicate the ability to achieve and maintain an erection sufficient for sexual activity, were improved up to 74% and 77%, respectively ($p<0.01$).

It is very important to note that despite the marginal improvement in sexual desire (20%) that is of psychological nature, great improvements were reported in the domains directly related with erection that is of physical nature and dependent on normal vascular function of the penile artery.

Also noteworthy, was a significant increase in the orgasmic function score

(87%), intercourse satisfaction (74%) and overall satisfaction (62%) as well as erectile function (66%) in comparison with the results for sildenafil reported by Marks, et al. *(Marks, et al., 1999)* (27%, 44%, 39% and 66%, respectively), which indicates that ECE significantly contributed to the normalization of the general vascular conditions around the sexual organ.

These results strongly indicate that the long-term administration of ECE significantly contributes to the neutralization of oxidative risk factors, thereby improving peripheral blood circulation around muscles and nerves involved in sexual function as well as the penile artery. No side effects were reported.

Vasodilation & Erectile Function

It has been reported that vasculogenic ED patients have elevated levels of angiotensin II for the duration of the erection process. The demonstrated action of ECE on ACE and resulting vasodilation is thought to play an important role in inducing successful erectile function.

Long-Term Improvement Via Vascular Protection

As discussed, ECE phlorotanins have potent antioxidant and anti-inflammatory effects. Together with ECE's ACE inhibitory activity, which is also beneficial to vascular homeostasis, these activities, upon long-term oral administration, may all contribute to supporting a healthy vascular system, including the penile artery.

WEIGHT LOSS

DGAT Inhibition

Diacylglycerol acetyl transferase (DGAT) is the enzyme involved in the final step of triglyceride synthesis. Triglycerides are circulating fat bodies that ultimately wind up in the fat cells, and are almost always elevated in diabetes. They also have emerged as a major risk factor in vascular disease.

Dr. Lee found that ECE compounds inhibited DGAT more than 50%. In genetically caused obese laboratory rats, ECE reduced body fat and increased physical activity. In another study, ECE caused leanness and fat-resistance in animals given a high fat diet.

ECE Beverage: 2-Week Clinical Trial

In a human study, 141 young adults were given a beverage containing ECE at 200 mg daily. In two weeks their average weight dropped nearly 2.5 pounds, muscle mass increased by nearly 2.5 pounds, and body fat dropped by 4 pounds, or 7.48%. ECE stimulates the body to burn fat by increasing muscle mass.

OBESITY

Obesity & Cardiovascular Disease

As discussed, ECE contains an optimal combination of natural compounds capable of suppressing triglyceride synthesis, while promoting cholesterol removal and cardiovascular protection. ECE provides additional cardiovascular protection for obese patients prone to CVD and CHD through lowering LDL cholesterol and scavenging free radicals.

DGAT Inhibition & Obesity

DGAT inhibition has recently been recognized as a novel and safe target for the treatment of obesity. DGAT is involved in intestinal fat absorption, lipoprotein assembly, regulation of plasma TG concentration, fat storage in adipocytes, and energy metabolism in muscle. DGAT knockout mice have been shown to have obesity resistance with a high-fat diet, the mechanism of which was confirmed to be through energy expenditure.

DIABETES

Aldose Reductase Inhibition

When blood sugar levels become elevated, aldose reductase is the enzyme that converts excess glucose into the sugar alcohol sorbitol. Sorbitol can build up in critical cells and cause damage. Recent research found that animals deficient in aldose reductase were protected from the retinal complications of diabetes. ECE compounds have been found to be potent aldose reductase inhibitors, which may be of benefit for patients with metabolic syndrome, syndrome X, or diabetes.

Reduced Fat in Liver & Pancreas

A mouse study showed that ECE reversed fat deposition in liver and pancreas cells. Furthermore, this same study showed that ECE served to markedly inhibit NF-kappaB inflammation in the pancreas. A recent Harvard (Joslin School of Diabetes) mouse study directly implicates excessive fat deposition in the mouse pancreas as turning on the NF-kappaB inflammation pathway, resulting in full-blown type II diabetes and insulin insensitivity in the mice.

SAFETY

ECE is manufactured from edible algae through food-compatible processes. Tens of thousands of people throughout the world have experienced ECE in various forms of product without side effects. To date, Dr. Lee's team has not found any toxicity at any level. Several toxicity tests have been performed, and no adverse effects have been found at the effective human dose level of 1-10 mg/kg. ■

References available on request.

Traditional Vietnamese Herb *Crinum Latifolium* Shows Promise for Prostate & Ovarian Health

by Stephen Levine, Ph.D.

Crinum latifolium shows promise to become one of the leading treatments in the world for benign prostate hypertrophy (BPH) and ovarian conditions, including polycystic ovarian syndrome. Its benefits for prostate cancer should be explored.

"I have found Crinum to be universally effective for several patients with ovarian cysts." **– Dr. Abram Ber, M.D.**

Traditional Vietnamese Herb

One of Vietnam's most potent and effective medicinal herbs for prostate and ovarian health, *Crinum latifolium*, has recently come into the spotlight. Used traditionally for longevity, Crinum was so revered in Vietnam that it was reserved only for royalty, and commonly referred to as the "Medicine for the King's Palace" and the "Royal Female Herb." These traditional nicknames highlight one of Crinum's most unique aspects - its ability to target both prostate and ovarian health conditions. As clinicians well know, it is quite unusual for an herb to be effective for both men and women's health conditions, but Crinum appears to be effective for both. Crinum's benefits have also been reported to extend beyond prostate and ovarian health.

Benign Prostatic Hyperplasia

Crinum has been shown to alleviate the symptoms of Benign Prostatic Hyperplasia (BPH) (enlarged prostate). BPH is one of the most common male health conditions, the main symptom of which is frequent and sometimes painful urination. There are over 500 successful case histories using Crinum for BPH. After seven years of research, the International Hospital in Vietnam reported that 92.6 percent of BPH patients had good results using Crinum (confirmed by measurements of prostate size and clinical evaluations by urologists).[1] The doctors used the extract for 21-day cycles, with 7 days off in between. They reported no side effects and no lethal level in animals (meaning incredible safety).

One of the study patients, a 72-year-old man, had suffered from BPH symptoms for three years, waking up 4-5 times per night with difficult urination. He was evaluated at the International Hospital, and diagnosed with BPH with prostate dimensions of 4.1, 5.4 and 4.8 cm, with a weight of 53 grams. Previously, he had been advised to have his prostate removed, but because of a hypertensive condition, he tried a Crinum protocol instead. After only three cycles of treatment (21-days each), his prostate dimensions reduced to 2.9, 4.2 and 3.6, with a weight of just 22 grams. All his symptoms resolved and he reported feeling healthy.[1]

The International Hospital research was highly praised by the Vietnamese Health Ministry, and The National Health Committee declared Crinum to be the most promising area of research for the treatment of BPH.

In a Vietnamese study, 158 BPH patients were given a Crinum-based herbal preparation two times per day. After 64 days, patients were evaluated by clinical and ultrasound examinations. Researchers found that prostate size returned toward normal in 154 patients (97%). A three-year follow up confirmed a high rate of long-term success for those patients who completed therapy.[2]

In a recent report from the Vietnamese Central State News Agency (September 2005): *Crinum latifolium extract has a very good therapeutic effect on benign hyperthrophy of prostate (BHP)*, the National Institute of Traditional Medicine, the Institute of Traditional Medicine of Ho Chi Minh City, and the Institute of Aging Disorders of Hanoi tested Crinum in a large number of patients (627 patients) with BHP. The results have shown a 33-93% reduction in urinary symptoms. 90% of the tested patients achieved a reduction in prostate size. Among them a significant number of patients achieved a normalization of prostate size and urinary health after three months of therapy. There were no significant adverse reactions.[3]

The Hoang Family of Doctors

Although most of the research available on Crinum focuses on the prostate gland and men's health, much of the early research using Crinum for ovarian cysts was reported by the Hoang family of medical doctors. The Hoang family is made up of three generations of progressive Vietnamese physicians who have shared their research with each other and worked together to move the uses of Vietnamese and Chinese herbs to a new and innovative level in modern alternative medicine. Dr. Kha Hoang was the grandson of the Chief Teacher for the Vietnamese royal family and was responsible for making Crinum a "national treasure" for prostate and ovarian health. In 1984, Dr. Hoang's daughter had so many ovarian cysts that she was scheduled for surgery. But instead, Dr. Hoang put her on a Crinum tea protocol, and six weeks later, her cysts were gone. In all, the Hoang family of doctors have used Crinum combined with other herbs to successfully treat well over one hundred patients with ovarian and prostate conditions, and to date have reported a high success rate.[4]

Ken's Story

Ken Malik is the Co-Founder and Executive Director of the Prostate Awareness Foundation, a San Francisco-based non-profit organization that offers support, information, and resources for prostate cancer patients.

In his own personal battle with prostate cancer, Ken Malik decided to take the natural approach - opting for nutritional protocols and lifestyle modification. He had been using the herbal supplement PC Specs for eight years and found that it stabilized his condition. PC Specs had been marketed as an all-natural herbal formula, and had shown remarkable results for prostate conditions. But recently, it was pulled from the market after researchers found that certain PC Specs products actually contained synthetic and potentially harmful substances. Ken was one of thousands of men worldwide who were negatively affected when PC Specs was pulled off the market. After discontinuing the product, Ken's PSA levels slowly began to rise, so he began his search for a replacement. This is when he found Crinum.

Ken started taking Crinum, along with a number of other supplements, in January of 2002, and over the course of ten months, his PSA levels continued to rise, however his biopsies showed his prostate to be completely free of cancer cells. (Ken's rise in PSA levels coupled with normal biopsies is just one more report that adds possible credibility to recent claims that PSA testing may not be an accurate assessment tool for diagnosing and tracking of prostate cancer.)

Ken was so excited about his personal results with Crinum that he organized an informal trial with ten members of The Prostate Awareness Foundation. Participants took a proprietary Crinum formula daily for three months, and all ten reported some level of functional improvement.[5] (To view a recap of this informal trial go to: www.prostateawarenessfoundation.org)

The Prostate Awareness Foundation (PAF) is an educational foundation that provides men and their families with non-biased, patient-driven information on prostate health issues and treatment options. The foundation places an emphasis on lifestyle changes, diet and supplements as preventative measures. They also provide free-of-charge consultations, a support group program, monthly bulletins and a mentor program. PAF recommends an integrative approach to prostate problems using the best from both conventional and alternative medicine and encourages men to take proactive responsibility for their health and healing.

Currently, Ken continues to use Crinum daily, and also takes artemisinin, as well as a number of other supplements, which he rotates seasonally. Although his last biopsy in 2005 showed microscopic traces of prostate cancer, Ken reports that his cancer does not appear to be progressing. To date, Ken has lived a healthy, active life with prostate cancer for over eleven years. During that time, Ken's PSA levels have been as low as 2.1 and as high as 19.1. Ken notes that he has learned to live with what he sees as a cyclical rhythm to his PSA, and does not become alarmed at a high readings, but instead, looks for trends. This is a novel perspective and needs to be further explored.

Crinum for Women

There is much less data available on the use of Crinum for women's health conditions. However, as Crinum becomes more popular, new data is emerging. Below are some very promising case histories from prominent doctors on the use of Crinum for polycystic ovarian disease.

Polycystic Ovarian Syndrome

Dr. Thomas Dorman, M.D.

Case History: Dr. Dorman recently had a female patient with polycystic ovarian syndrome (PCOS). Her symptoms included irregular periods, decreased sex drive, weight

gain, and excessive facial hair (from excess male hormones, confirmed by a laboratory), all of which are quite common in PCOS. After only two months on a Crinum formula, as a single intervention, her menstruation and weight normalized, her facial hair diminished, and her sex drive returned. There has now been nine months follow-up without a deterioration in this regard.[6]

Dr. Abram Ber, M.D.

"I have shared this case history to confirm the efficacy of Crinum latifolium. I have found it to be universally effective for several other patients with ovarian cysts." – Dr. Abram Ber, M.D.

Case History: C.G. is a 39-year-old woman who has polycystic ovaries as a part of the complex Syndrome X. She developed menorrhagia and her gynecologist referred her for a pelvic sonogram on 4/26/05. She subsequently had a visit in my office and I prescribed *Crinum latifolium* 3 caps tid. She began to take the Crinum capsules over the Memorial Day weekend and felt twitches in the area of her right ovary. 3-4 days later, she had a fever of 103, which lasted for three days. During these days she was anorexic. After the fever, she was ten pounds lighter. This weight loss was very welcome and the weight was not regained. On June 16, 2005, a repeat pelvic ultrasound showed a complete resolution of the previously described complex cyst. She now feels wonderful and relieved of all symptoms pertaining to the cyst.[7]

Dr. Graeme Shaw, M.D.

Case History: A 52-year-old woman in perimenopause was evaluated by her gynecologist for heavy periods and was diagnosed by pelvic ultrasound as having a uterine fibroid tumor and multiple bilateral cysts. Her gynecologist suggested ovarian surgery, but she requested a trial on natural supplements and was placed on a Crinum compound (3 caps 2x per day). Seven weeks later, she had a repeat pelvic ultrasound and there was no evidence of any cysts, and her surgery was cancelled.[8]

Speculations About Mechanism

The Crinum plant is a large tropical plant with lily-like flowers that is found in the tropical and subtropical regions throughout the world. Phytochemical analysis has recently yielded a vast array of compounds, including more than 150 different alkaloids of the Amaryllidaceae plant family, whose most noted effects are analgesic, anticholinergic, antitumor and antiviral.[9] While numerous successful case studies exist, researchers are still not sure exactly how Crinum works. Some researchers believe it may enhance the cellular communication that is responsible for maintaining the balance between cellular proliferation and apoptosis. Without this check and balance system, unhealthy cells may be left to proliferate. Recent research has shown that Crinum encourages cells to produce a substance called neopterin, which is responsible for communicating with immune cells - calling them into action against foreign invaders and unhealthy or proliferative cells. This suggests that Crinum may not only be valuable for prostate and ovarian conditions, but may also be beneficial for other conditions in which unhealthy, proliferative cells are involved. Crinum has been shown to be a strong immune stimulant based on the research of Drs. Nguyen Ngoc Tram, Do Tat Loi, D. Fuchs (Austria), Dr. Popov and Zvekova (Bulgaria).[10] Dr. Ba Hoang, M.D., Ph.D. also states that in Vietnam, Crinum has been used successfully for hot flashes, as well as tonsilitis, laryngitis, and cough.

Crinum May Offer Protection

Another potentially valuable benefit of Crinum is that it may be used as a preventative agent, offering protection against prostate and ovarian conditions before they start. ■

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The Strange Case of Strontium

A Reason-Based Editorial by Daniel Milosevich, CN, with Stephen Levine, Ph.D.

It is widely known that the new drug strontium ranelate offers a new option for drug treatment of osteoporosis. Now, various nutritional experts are recommending the trace mineral strontium as an essential nutrient for bone health, based on the research for the drug strontium ranelate. By ignoring the fundamental differences between drug activity (disease treatment) and nutritional support (benefiting the body's structure and function), these writers have created two misconceptions: that strontium in high milligram doses is essential for bone health; and that nutritional strontium must be taken on an empty stomach. What is worse, everyone seems to have missed an obvious reason why ingesting a trace mineral in abnormally high amounts can increase bone mineral density – and what it is replacing. A reasoned look at strontium offers some surprises about how to safely use it nutritionally.

Osteoporosis is not caused by strontium deficiency, and good bone health does not rely on excessive strontium. The health of the bones is due to multiple interacting causes, and there is not a single drug or nutrient that is the key to the health (or disease) of the bones. Nutrients that support dense, strong bones are interdependent, and all are needed for optimal bone growth and strength. They include calcium, magnesium, vitamin D, vitamins K1 and especially K2, vitamin C, potassium, copper, manganese, zinc, silicon and boron. Real nutritional support for bones will account for as many of these factors as possible, rather than focusing on one magic ingredient. Healthy bones also depend on hormonal balance resulting from good endocrine system function, balance among macronutrients (protein, fatty acids, sugars), and appropriate exercise.

Drug developers, on the other hand, must look for one ingredient – or a way to utilize one ingredient – that can be shown to make a difference in a disease state. The novel compound strontium ranelate is composed of one part ranelic acid and two atoms of stable strontium. According to Dr. Reginster, a lead strontium ranelate researcher, it was chosen because it presented the most suitable physicochemical and pharmacokinetic characteristics, and was well tolerated and safe (although many other strontium salts also are well tolerated and safe). Undoubtedly, strontium ranelate was preferred over other known (and researched) strontium salts because, as a previously unknown form of strontium, it could be patented.

The confusion of strontium ranelate with the nutrient strontium partly stems from the fact that even Dr. Reginster admits that the strontium is the effective part of the compound, saying, "Certainly, the ranelic acid part of the strontium ranelate compound contributes nothing to the effects of strontium on your bones." This implies that other forms of strontium could potentially have the same benefits, and nutritional writers were quick to extol the potential benefits of strontium without looking closely at what can really be logically extrapolated from the strontium ranelate research to the use of nutritional strontium.

A Closer Look at Strontium

Strontium is a trace mineral, typically ingested from food and water at 1-3 mg per day, although much less is absorbed. It may have some essential function as a trace mineral in the bones, although this is unverified. Trace amounts of strontium reside in the skeleton for years, replacing a small amount of calcium in

Living Bones

The growth and development of the skeleton begins in early fetal life and continues for nearly two decades in a series of well-defined events. Minerals, particularly calcium, but also carbonate, magnesium, sodium, and fluoride, play vital structural and metabolic roles in bone growth and development. However, bone formation also is encouraged by hormones, such as estrogen, and by weight-bearing activity. Living bone is never metabolically at rest; its matrix and mineral stores are being remodeled constantly along the lines of mechanical stress.

Home Care Provid. 1997 Apr;2(2):76-81; quiz 82-3.

the hydroxyapatite crystal lattice. This nutritional strontium is ingested with, and competes for absorption with, all the other elements that occur in food and water, yet the body has no problem making use of it at these levels.

In the research on strontium ranelate, the test subjects first normalized their vitamin D and calcium levels, and continued to take calcium and vitamin D during the time that strontium was taken. Because the absorption of strontium ranelate is reduced significantly by the presence of calcium or food, the drug was taken on an empty stomach. Strontium taken in this way can be adsorbed onto the surface of hydroxyapatite crystals, and this is probably where the increases in bone mineral density (BMD) occur. But because only a small quantity of calcium in the apatite is substituted by strontium at these pharmacological doses, once high-dose empty-stomach strontium treatment is withdrawn, bone strontium levels rapidly decrease. The drug researchers claim that the body targets the bones with strontium, but the body may simply be storing the excess there until it has an opportunity to get rid of it.

Strontium's Secret

Millions of human beings have grown old with strong, healthy bones without loading up on strontium. Could it be that something else was low in the test population, something that excessive strontium can partially replace? Consider these points: 1. Magnesium is typically below optimum levels, or even deficient, in the population at large. 2. Osteoporosis can be considered a further risk marker for magnesium deficiency. 3. Giving extra calcium to already magnesium-low subjects will exacerbate any magnesium deficit. Since no attention was paid to magnesium status in any of the strontium ranelate studies, and all subjects had osteoporosis, and extra calcium was given, it's almost certain that the general level of magnesium was sub-optimal at the least, and more likely, outright deficient in the population tested.

Strontium may possibly help stabilize mitochondrial structure, but magnesium is known to have critical importance for stabilizing mitochondrial structure. Strontium has some ability to enhance calcium deposition in bones, but magnesium already does this wonderfully. Strontium is said to be a "bone-seeking element that is closely related to calcium", but magnesium is the other mineral "closely related to calcium", and is not only bone-seeking, it is bone-residing: a healthy adult human skeleton contains 15-17 grams of magnesium. Magnesium is crucial for many body systems, but especially for bone formation and mineralization. In my opinion, high-dose strontium's 'secret' is that it can partially ameliorate magnesium deficiency, filling in for magnesium's superb ability to increase bone growth, bone density, and bone strength.

Is magnesium that important? Don't we all get enough magnesium?

Increased bone mineral density and bone mineral content in postmenopausal women have been positively correlated with intake of supplemental and/or dietary magnesium. Women with postmenopausal osteoporosis show significant reductions in bone mineral content

Magnesium Crucial for Bones

There are hundreds of studies showing the crucial role that magnesium (Mg) plays in the health of the bones. For example, although severe Mg deficiency has long been known to be a risk factor, what happens with just a moderate Mg deficiency? Rats fed 0.04% of the nutrient requirement (NR) for Mg (severe Mg deficiency) get osteoporosis. A more moderate dietary Mg restriction, 10% of NR, was then tested for six months. After just two months, bone Mg content was reduced 51%. Increased release of substance P and TNF-alpha were noted by the end of the study and bone loss. J Nutr. 2004 Jan;134(1):79-85. Then 25% of NR was tested, and again decreased bone volume occurred. "These data demonstrate that Mg intake of 25% NR in the rat causes lower bone mass which may be related to increased release of substance P and TNFalpha." Bone. 2005 Aug;37(2):211-9. Recently a very moderate reduction of dietary magnesium (50% NR) was tested. As found in more severe Mg restriction, bone magnesium content was reduced at the 3- and 6-month time points, as was bone volume. Osteoporos Int. 2006;17(7):1022-32. Epub 2006 Apr 7. Other studies confirm a similar role for magnesium in humans. Rats given half their needed magnesium suffered bone loss in 6 months. How many millions of human beings are subject to chronic, long-term 50% (or less) intake of optimal magnesium? Why are we surprised at the near-epidemic of osteoporosis?

See more magnesium references and commentary at:
www.allergyresearchgroup.com/news/letters/srreferences.htm

and serum magnesium compared to age-matched controls. Insufficient magnesium stops bone growth, and leads to osteopenia and bone fragility. Magnesium makes bones and teeth dense, strong, resilient (not brittle), and hard.

Research indicates dietary intake of magnesium has decreased in the United States, from 475-500 mg per day in 1900, to only 215-283 mg per day in 1990. Even those 1990 figures may be too high, since refining and cooking further reduce the magnesium content of foods. A high-fat diet, soft drinks, laxatives and many other common dietary practices all can seriously compromise magnesium absorption and retention. Other factors, such as high alcohol or sugar intake, elevated stress chemistry in the body, diuretics or high amounts of sodium or calcium can reduce re-absorption of magnesium in the kidneys. Additionally, acid rain washes magnesium out of the soil, fluoridation depletes it from drinking water, and the processing of grains and other foods lowers their magnesium content. A 1988 U.S. Government study concluded that the Standard American Diet (SAD) only provided 40% of the daily requirement of magnesium. Some experts believe this is a major root cause of the myriad chronic health conditions suffered in the modern world.

It's quite possible that a low-magnesium diet combined with high calcium intake will promote calcification of soft tissues and create an environment for osteoporosis to begin. Interestingly, the research also shows that increasing magnesium intake improves rather than interferes with calcium utilization. Magnesium regulates active calcium transport, crucial to bone metabolism. Plentiful magnesium is calcium-sparing, reducing the need for calcium.

Quality Bones

In a two-year study of postmenopausal women with osteoporosis, 170 mg of strontium per day reduced bone fracture risk more than the 680 mg dose used in the other studies, even though BMD did not increase as much at the lower dose. With the higher strontium dose, even as BMD increased, over time the fracture risk also started to increase again. Does either of these make sense if high quality bone were being formed?
It appears that bones deficient in magnesium and high in strontium, although very dense, are not as strong as bones with optimal magnesium content. The body is making do with what it can get, akin to soldiers armoring their vehicles with scrap metal. The vehicles are somewhat more bomb resistant (less prone to fracture), and certainly heavier (denser), but not as bomb resistant as those outfitted with high-grade armor (optimal magnesium). This makes sense, as the excess strontium is absorbed onto the surface, not the deep crystal lattice.

What other functions do strontium & magnesium have?

Both magnesium and calcium, unlike strontium, are involved with hundreds of activities in human metabolism. Magnesium plays a role in the cardiovascular and GI systems, peripheral vascular function, energy production, and the heart, brain, kidney and liver. It is involved in the regulation of muscle and nerve activity through influencing cell membrane permeability, and functions as an electrolyte, helping maintain the charge balance in the body fluids. Magnesium governs the flow of sodium, potassium and calcium in and out of cells, and complements calcium. Strontium, on the other hand, is found exclusively in the bones and teeth in minute amounts, with no verified essential functions.

Do the large doses of strontium used in the studies pose any danger?

Strontium ranelate has been shown to increase BMD and reduce fracture risk in postmenopausal women, with pharmacological doses of 680 mg strontium per day, (but magnesium levels were not tested, or optimized, in either the test group or the controls). It is likely that these large doses of strontium are not dangerous, as long as calcium stores are maintained. Skoryna, an original researcher on calcium and strontium salts, wrote, "Supplementing a diet that provided the usual amount of calcium with stable strontium… demonstrated that there is a wide margin of safety in the amount of stable strontium intake in human subjects, since doses of up to 1750 mg/day of strontium ion did not produce any side effects." However, he goes on to say that both high strontium/low calcium diets, or massive doses of strontium (1.5% to 3% of the dietary intake) can lead to a pathological decrease of bone calcium originally described as "strontium rickets". Excessive strontium intake has also been reported to produce

Continued next page

insoluble phosphates, leading to phosphorus deficiency.

Those that advocate the use of large amounts of nutritional strontium on an empty stomach may not be considering these safety issues. For example, a senior citizen could start taking high-dose nutritional strontium twice a day, thinking this is what she needs for her osteoporosis, without understanding the need to keep her calcium and vitamin D stores up. Even if she is told to take calcium, she may forget, she may get confused, or there could be other reasons why she stops taking calcium. Such compliance issues are common. Over time, she could create serious problems for herself. The safety of nutritional strontium can only be assured when it is taken with calcium, magnesium, and other nutrients important for bone health.

Conclusion

For those who have no interest in optimizing their nutritional intake, and want to take one thing to cure their osteoporosis, the research suggests that the drug strontium ranelate may strengthen bones as well as, or possibly better than, any of the other drug treatments currently available, as long as they keep taking it, and take adequate calcium and vitamin D.

For those who wish to support the normal corrective processes that result when the body and bones are viewed as a complex system, attention would be paid to exercise, hormones, a balanced diet, and improved overall nutritional status. Emphasis would be placed on a daily intake of vitamin D, vitamins K1 and K2, vitamin C, lycopene, and a full array of minerals including calcium, magnesium, zinc, copper, manganese, strontium, silicon and boron. There is no need to trick the bones into absorbing physiologically abnormal amounts of strontium. There is also no requirement to take nutritional strontium on an empty stomach, and significant reasons not to do so. The strontium in such a program may support a speedier if temporary bulking of bones that are in dire need, while the body continues to build real bones with the macro nutrients calcium and magnesium. Strong, healthy bones do not need large amounts of nutritional strontium, but they will always require plenty of magnesium. ■

References available at:
www.allergyresearchgroup.com/news/letters/srreferences.htm

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