Super Antioxidant from the Sea: More Potent than EGCG from Green Tea

Ecklonia Cava Extract (ECE), a polyphenol/phlorotannin rich nutraceutical, is derived from a specific species of brown algae *Ecklonia cava*. Over 30 million dollars has been spent on research, which has presented intriguing treatment leads, stemming mostly from ECE's powerful antioxidant function, for much of present-day illness. ECE offers nutritional intervention for fibromyalgia, hypertension, sexual and erectile dysfunction, memory enhancement, relaxation and alertness, deep sleep, allergies, asthma and lung disease, cardiovascular health, arthritis, neuropathy, weight loss, increased muscle mass and obesity, Syndrome X, and diabetes.

**Fibromyalgia Phase I Clinical Trial Results**

(Preliminary)

A preliminary Phase I study of established fibromyalgia (FM) patients was undertaken with an original recruitment of 36 patients and completion by 29 patients.

1. sleep: mean time to sleep (<47 min, p<.024), amount of sleep (+1.6 hrs/night, p<.001), soundness of sleep (+80%, p<.01);
2. fatigue (-30%, p<.001);
3. energy (+71%, p<.001);
4. number of “good days” (+56 hrs/week, p<.001); number of lost “work” days/week (-31 hrs/wk, p<.001);
5. pain (-31%, p<.001); and
6. global assessment of general condition (+39%, p<.001).

A strong dose-response relationship was not established at statistically significant levels. ECE was concluded to offer reasonable safety and statistically significant improvement in symptoms for most of the study population over the eight-week trial period (Figures 1-7).
The Molecular Structure of ECE Compared with other Polyphenols

Resveratrol
Resveratrol belongs to a well-known class of phytochemicals called flavonoids. Flavonoids and related compounds are called polyphenols. A phenol is a simple ring chemical.

Quercetin
Polyphenols are phytochemicals (plant-made) with multiple, interconnected phenol rings. Flavonoids have a typical three-ring structure as seen in Figure 8.

Green Tea Catechins
Catechins from green tea have four rings (corresponding to their four peaks under high-pressure liquid chromatographic ["HPLC"] analysis) (Figure 9).

ECE Compound Dieckol
Newly discovered class of polyphenols extracted from the Ecklonia cava seaweed, collectively called "ECE." Two of ECE's more than 13 active fractions (dieckol and PFF) that are particularly important are provided in Figures 10 and 11.

Figure 10: Dieckol Structure

ECE Compound phlorofurofucoeckol (PFF)
The ECE compound phlorofurofucoeckol (PFF) has a very complicated molecular structure and a doubling of the rings, which explains its powerful antioxidant activity (Figure 11). When combined with a much longer in vivo effect, ECE's free radical scavenging ability is ten to 100 times more powerful than land-based polyphenols, far exceeding resveratrol and green tea catechins.

Figure 11: PFF Structure

Fat-Soluble Polyphenol
Water-soluble compounds have less ability to penetrate the blood brain barrier. ECE compounds are 40% lipid soluble (i.e., "hydrophobic"). This means ECE has the ability to penetrate the blood-brain barrier, implying greater ability to get into and protect the brain. It also means a much longer half-life in the body, up to 12 hours compared to 30 minutes for most water-soluble polyphenols. The difference in half-life is considered to be one of a few key factors in determining its enhanced antioxidant effects.

ACE Inhibition
ECE compounds can potently suppress Angiotensin-Converting Enzyme (ACE). In a rat study, the renal artery was clipped, stimulating the organ to make the hormone rennin, which in turn stimulates ACE to increase blood pressure. ECE was compared to the drug enalapril (Vasotec); it showed a similar blood pressure-lowering profile. But unlike the rats given the drug, ECE rats did not show the rebound in blood pressure when the product was stopped. ECE has more than 15 times the power to inhibit ACE as the most powerful land-based polyphenols.

ECE Comparable to Viagra®
Nitric oxide (NO) dilates blood vessels. After six weeks of ECE treatment, flow-mediated dilation and NO-mediated dilation increased by 60% and 50%, respectively. This means ECE can rejuvenate damaged endothelial cells. This effect was further confirmed in a study on

Figure 7: Reduced Work Days Lost by 40%
Ecklonia Cava Extract

erectile dysfunction (ED). In an eight-week study on 31 men with ED for more than six months, ECE was compared with the drug Viagra® in the following parameters: orgasmic function, intercourse satisfaction, overall satisfaction, and erectile dysfunction. ECE scored 87%, 74%, 62%, and 66%, respectively. Viagra® scored 27%, 44%, 39%, and 66%, respectively. No side effects were reported.

Neuropathy
The strong lipid and cholesterol scavenging potential of ECE to "scrub" the endothelial lining of plaque in the blood vessels and arteries provides a further additional benefit: reduced vasculitis (i.e., vascular inflammation). Increasingly, the scientific literature supports the notion that many forms of nerve pain ("neuropathy") are caused by nerve pressure, as exerted by swollen, inflamed blood vessels adjacent to the nerves. A recent 40-patient, placebo-controlled, randomized clinical trial on neuropathy confirmed ECE's ability ("NeuralPlus®") to reduce nerve pain by 40% in four weeks of daily dosing, with an 80% response rate.

Brain Support
Dr. Lee's study found that the velocity of blood flow into the carotid arteries can be increased from an average of 36.68 cm/sec. to 40.09 cm/sec, while the placebo group had no improvement. An EEG study on brain waves of healthy, middle-aged volunteers found that ECE compounds increase alpha waves, an indicator of relaxation. Yet another study found that ECE compounds prevented sleepiness in bus drivers and in high school students during daytime activities.

Asthma, Allergic Lung Disease, and Chronic Obstructive Pulmonary Disease
In a mouse study, Dr. Lee's team found that allergic inflammation was significantly reduced. Specifically, the migration of eosinophils to the lungs was reduced by 75%; inflammatory white blood cells were reduced by 50%; mucus plug in airways was reduced by 50%; the increase in number of airway epithelial (lining) cells was reduced by 75%; and collagen (fibrosis) in lung tissue and smooth muscle cell thickness was reduced by 20% and 32%, respectively. These latter findings suggest that ECE compounds can prevent or reverse the chronic progression of asthma and potentially even Chronic Obstructive Pulmonary Disease (COPD).

Arthritis, Pain, and Atherosclerosis
ECE significantly reduced pain in a group of knee arthritis patients compared with placebo. Oxygenase enzymes called LOX (lipo-oxygenase) are related to the generation of allergies, atherosclerosis, and some cancers. ECE compared almost identically to celecoxib (Celebrex) in the ability to reduce PGE2 by slowing down the LOX system. Its compounds have more than double the ability of resveratrol to inhibit LOX. The benefit was demonstrated in a study on rabbit cartilage cells. Those cells fed ECE had up to an 80% reduction in degeneration.

Sleep and Alertness
Considering the improvement in sleep for fibromyalgia patients and the increased alertness for high school students and bus drivers, ECE appears to be stimulating ideal function: increased alertness when you need it and increased ability to sleep when you need it. The more than 50 million Americans with various sleep disorders might well benefit from ECE, without the fears of addiction present with prescription sleep aids.

Radiation and Cancer Protection
Dr. Lee conducted a study on the effects of ECE compounds on mice exposed to UV rays. Mice were given either oral or topical ECE and then exposed to UVB, a toxic ultraviolet wavelength. The results were remarkable. Tumor cell division was reduced by 50%. The inflammatory chemical PGE2 was reduced by 50-80%. COX2 and other inflammatory enzymes were significantly reduced.

Inhibitor of Aldose Reductase
High blood sugar leads to vascular complication. One way that happens is through an enzyme called aldose reductase (AR). This enzyme is present in the eyes, nerves, and many other parts of the body. It becomes dangerous when blood sugar gets too high. It converts some of the excess glucose into the sugar alcohol sorbitol. Sorbitol can build up in these critical cells and damage them. In fact, recent research found that animals deficient in AR were protected from the retinal complications of diabetes. ECE compounds are potent inhibitors of this enzyme. Hence, patients with metabolic syndrome, syndrome X, or frank diabetes, would benefit from ECE.

Obesity
ECE might naturally prevent fat accumulation. In a mouse study, ECE inhibited diacylglycerol acyltransferase (DGAT), reduced blood sugar, reduced fat cells and fat resorption, and decreased the number of fat cells during the feeding period. ECE induced a 30% reduction in blood vessels to fat tissue [angiogenesis] and significantly reduced lipid contents in skeletal muscles and around blood vessels. Obese mice lost more than ten percent of their body weight in 120 days. The animals suffered no side effects, had shiny skin, and were more active and alert.

Reduced Fat, Increased Muscle
ECE compounds can inhibit DGAT more than 50%. In mice, suppressing DGAT led to reduced body fat and increased physical activity. But most important, it encouraged leanness in animals and resistance to a high fat diet. One hundred and forty-one young adults were given a beverage containing ECE at a daily dose of 200mg/D. In just two weeks, average weight dropped over 1.09kg.
muscle mass increased over 1.13kg, and body fat dropped 1.86kg. Body fat in this group dropped a stunning and highly statistically significant 7.48%. ECE blocks fat creation and stimulates its combustion via increase in muscle mass.

Reduced Fat in Liver and 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-kB 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-kB inflammation pathway, resulting in full-blown type 2 diabetes and insulin insensitivity in the mice. It makes sense that a substance that reduces pancreas fat accumulation might restore insulin production and reverse type 2 diabetes.

Atherogenic Index Drop

If insulin metabolism is impaired, lipid and cholesterol metabolism will also be impaired. Thirty-nine adults average age 55.6 were given 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%. Although some of these individual changes were quite moderate, all were in a therapeutic direction. These results were achieved with no changes in lifestyle.

Summary of ECE

- Strong elastase agonist effect, thereby increasing the flexibility of the vascular system and helping normalize blood flows and blood pressure
- Significant anti-inflammatory effect, by inhibition of the Nf-kB inflammatory pathway, which also serves to normalize blood glucose levels and lead to statistically-significant re-establishment of insulin sensitivity in the pancreas
- Downregulation (by 60%) of the DGAT enzyme responsible for lipid (fat) metabolism, thereby assisting in fat/weight loss
- Significant analgesic effect in inhibiting the expression of the COX enzymes for arthritis, as well as for neuropathic and FMS/CFS pain
- Inhibition of beta-amyloid brain plaque formation as well as short-term memory in mammals, thereby improving overall memory function
- Anti-tumor effects (currently tested only for dermatologic cancers in mice)

Summary of Clinical Studies

- Hypertensive cardiovascular patients (reduction of blood pressure and increase of brachial artery FMD [+43%] and NMD [+59%] in CAD patients [11 of 39 patients, the others being healthy normals]
- Analgesia in osteoarthritic patients (comparable to the COX-2 inhibitors)
- Weight loss in both obese and normal patients
- Erectile dysfunction on males with ED (comparable to Viagra®)
- Analgesia in neuropathic pain patients (i.e., neuralgia)
- Major multi-symptom management (i.e., reduction in pain, fatigue, sleep disorders) for fibromyalgia patients.

References

**General**

Ecklonia Cava Extract


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Cardiovascular Support

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Erectile Dysfunction


Plasma levels of angiotensin ii during different penile conditions in the cavernous and systemic blood of healthy men and patients with erectile dysfunction. Urology. 2001;58(5).

Possible role of bradykinin and angiotensin ii in the regulation of penile erection and detumescence. Urology. 2001;57(1).


Fibromyalgia

Preliminary Clinical Report of ECE Phase 1a Clinical Trial Results, November 25, 2005 (Manufacturer's Study).

Brain Support/Immunity Enhancement


Arthritis/Neuralgia


Weight Loss/DGAT Inhibition


Immune Support


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