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Ecklonia Cava Extract:
Superior Polyphenol and Super-Antioxidant for Our Time

by Richard Bierman LAc, REA

If there ever was a need for a superior compound, this is the time, and Ecklonia Cava Extract (ECE) fills the need. With its wide-ranging biological activity, ECE has been shown to positively impact a whole host of maladies from inflammatory-mediated illnesses to erectile dysfunction.

ECE*, is a standardized natural complex of biologically active unique polyphenols called phlorotannins. These are categorized by a unique phenolic structure and low molecular weight found only in a few specific species of brown algae. This includes *Ecklonia cava*, the Japanese edible noro kajime.[1,2] ECE tannins are "super antioxidants" that have up to eight interconnected rings, making their free-radical scavenging ability ten to 100 times more powerful than any polyphenols found in land plants, including green tea catechins, which have three to four rings.[2] Phlorotannins found in *E. cava* include phloroglucinol, triphlorethol-A, eckol, bieckol, dieckol, and phlorofucoeckol. Extensive research, from *in vitro* through to Phase 1 trials, has shown ECE promotes a host of physiological activities with wide-ranging clinical applications. Some of these activities include superior antioxidant activity, vasodilatation, regeneration of vascular endothelial cells, fibrolysis promotion, anti-inflammation, prevention of LDL oxidation, mild acetylcholine (ACh) inhibitory activity, neuroprotective effects, erectile function enhancement, and DGAT inhibition.

* trademarked as Seanol®

Anti-Oxidative Effects

As a partially fat-soluble super-antioxidant, ECE not only can neutralize a great number of oxidative compounds, it can do so for longer periods of time as compared to lesser-ringed polyphenols. The estimated half-life of ECE is up to 12 hours, compared to 30 minutes for water-soluble polyphenols, such as EGCG in green tea.[3]

ECE shows exceptional scavenging ability of peroxynitrite, the free radicals 1,1-diphenyl-2-picrylhydrazyl (DPPH), and other Reactive Oxygen Species (ROS).[4] Research has shown ECE has a higher inhibition of LDL oxidation than catechins.[2] *In vitro* studies have shown that component compounds of ECE are very active in physiological relevant concentrations ranging from 10 to 20ug/mL. ECE is able to cross the blood-brain barrier.[2, 5, 6]

Anti-Inflammatory Effects

ECE shows strong inhibition of tissue-specific NF-kappaB and AP-1 activity, inhibitory action against MMP-2, MMP-9, and possible modulation of levels of PGE_2 and other prostaglandins. ECE has been shown to increase catalase, superoxide dismutase (SOD), and glutathione peroxidase activity, and modulate extracellular signal regulated kinase ERK pathways.[7-10]

Vascular Effects

ECE can restore endothelial cells, normalizing the production of nitric oxide acting as a vasodilator. ECE protects the cardiovascular system via promotion of fibrinolysis through antiplasmin inhibition and ACE inhibition.[11, 12]

Arthritis Inflammation Neuralgia Fibromyalgia

In an eight-week, double-blinded, placebo-controlled study of established fibromyalgia patients, ECE was used as an adjunct therapy to the patients' current standard of care. Preliminary results showed that ECE cut the time it took the participants to fall asleep by 47 minutes; increased total nighttime sleep by 1.6 hours; improved soundness of sleep by 80%; boosted energy levels by 71%; gave patients two-and-one-quarter more good days per week; helped reduce pain by 31%; and improved general condition by 39%. Interestingly, these improvements were achieved at all doses. No improvement during the study was found in the placebo group. The results also established the general safety of ECE.[13]

ECE's ability to treat arthritis was found to be comparable to Celebrex®, via reduction in inflammatory COX enzymes. A study evaluated ECE's impact on lipopolysaccharide (LPS)-induced generation of prostaglandin E2 (PGE2). All the compounds tested – celecoxib (Celebrex®), aspirin, and ECE – slowed down the lipooxygenase (LOX) system, showing significant inhibition of PGE2 generation.[2]

Inhibitory effects of phlorotannins on hyaluranidase, secretory phospholipase, several A2 cyclooxygenases

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and lipooxygenases have also been reported.[14, 15] In another study, ECE reduced nerve pain of 40 neuropathy patients by 40% in four weeks.[16]

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 spasmogens, compounds such as leukotrienes and 5-hydroxy-eicosatetraenoic acid. 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.[15]

Brain Function

In an animal study, ECE increased rodent acetylcholine (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. ECE may be involved in the upregulation of acetylcholine through mild acetylcholinesterase inhibitory activity.[17,18] Researchers 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.[19] ECE also contains fucoidan, which is found to protect neuronal cells.[20]

Researchers at the National Institute of Health's aging-research labs in Baltimore studied ECE in rats and found it inhibited beta-amyloid deposition in the brain. The rats also learned maze challenges faster, which demonstrated improvement in short-term memory.[21]

Allergies/Asthma

Allergic Inflammation: 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, at the 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 days 14-60. The antigen-treated and challenged mice developed extensive eosinophil and mononuclear cell inflammatory responses, mucus cell hyperplasia, and mucus occlusion of the airway. By feeding at a concentration of 5.4 mg/ml in the drinking water for 12 days, KLS reduced the airway mucus plugging by 75%, and airway epithelial hyperplasia was reduced by 75%. CD4+4 T Cells and resultant cytokines Il-4, 5, 13 were reduced by 50%. Collagen-causing fibrosis in lung interstitium (fibrosis, airway remodeling) and smooth muscle cell thickness was reduced by 20% and 32%, respectively. 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.[22] 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).

Cardiovascular Benefits

ECE has been shown to improve coronary artery disease (CAD). Researchers found that ECE is even more potent than green tea catechins at inhibiting the oxidation of LDL cholesterol and appears to scrub the plaque off the endothelial lining. ECE also reduces vascular inflammation by preventing oxidation, which also directly affects mediators such as inflammatory prostaglandins, etc.[2, 3, 23]

Coronary Artery Disease: Six-Week Clinical Trial, Reversing Atherosclerosis

A clinical trial using ECE confirmed its capacity to regenerate vascular endothelium and recover plasticity of blood vessels after six weeks of treatment by measuring flow-mediated dilation (FMD) and nitroglycerin-mediated dilation (NMD) vascular plasticity of normal and CAD patients with narrowed coronary arteries. After six weeks of treatment with ECE, clinical data showed that FMD and NMD were greatly enhanced in the CAD group by 43% and 49%, respectively. ECE has been shown to increase NO activity in the endothelium lining of the blood vessels.[23]

In the same study, 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%.[23] 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.

Hypertension: Four-Week Animal Study

The remarkable effect of ECE on vasodilation was also 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 four weeks. Upon oral administration of phlorotannin (99.4%, 50 mg/kg) or enalapril (commercial anti-hypertensive 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.[24]

ACE Inhibition

Angiotensin-converting enzyme (ACE) is responsible for conversion of angiotensin I to angiotensin II and degradation of bradykinin. Angiotensin II regulates cellular proliferation, inflammation, and endothelial function and is therefore important in the pathogenesis of atherosclerosis and its complications. 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 plant polyphenols, including catechins. One of the compounds found in ECE, THP-BE is comparable to the physiological vasodilative hormone bradykinin.[3, 24]

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 antiplasmin, capable of efficient promotion of plasmin. ECE compounds have shown remarkable activity that is 40-200 times greater than then Flufenamate. One study on ECE compounds found a small but significant rise in prothrombin time and a fall in fibrinogen levels.[11, 12]

Erectile Functionece Vs. Viagra®

ECE Vs. Viagra®: Eight-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%, respectively. Viagra® scored 27%, 44%, 39%, and 66%, respectively. No side effects were reported with ECE. These results strongly indicate that the long-term administration of ECE significantly contributes to the

Ecklonia Cava Extract

neutralization of oxidative risk factors, thereby improving peripheral blood circulation around muscles and nerves involved in sexual function as well as the penile artery.[5]

Erectile Dysfunction

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.[25]

Weight Loss

DGAT Inhibition

Diacylglycerol acetyl transferase (DGAT) is the enzyme involved in the final step of triglyceride synthesis. DGAT is involved in intestinal fat absorption, lipoprotein ➤

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assembly, regulation of plasma TG concentration, fat storage in adipocytes, and energy metabolism in muscle. DGAT inhibition has recently been recognized as a novel and safe target for the treatment of obesity. ECE reduced body fat and increased physical activity, and inhibited DGAT more than 50%. In another study, ECE caused leanness and fat-resistance in animals given a high-fat diet. ECE provides additional cardiovascular protection for obese patients prone to coronary vascular disease (CVD) and coronary heart disease (CHD) through lowering LDL cholesterol and scavenging free radicals.[26 27]

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. *In-vitro* data found ECE compounds to be potent aldose reductase inhibitors, which may be of benefit for patients with metabolic syndrome, syndrome X, or diabetes.[28]

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.[29]

Safety

ECE is manufactured from edible algae through food-compatible processes. Several toxicity tests have been performed, and no adverse effects have been found at the effective human dose level of 1-10 mg/kg.[30]

Richard D. Bierman L.Ac, REA is a licensed acupuncturist and a registered environmental assessor with a background in environmental and energetic medicine and chronic inflammatory diseases.

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