Chronic Fatigue | Fibromyalgia

TOWNSEND LETTER

The Examiner of Alternative Medicine

FEB/MARCH 2008

Celebrating 25 Years of Publication!

Cranial Electrotherapy Stimulation
The Brain and Fibromyalgia Pain

Multiple Chemical Sensitivity
When the World Turns Toxic

Amping Up Healing
Electromedicine Makes Sense

Statin Dangers
Debunking Cholesterol Myths

Tall People Have No Reason to Live...Longer
The Longevity Gap

74470 87090 6 02

#295/96 | $5.95

www.townsendletter.com

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

by Robert Jay Rowen, MD

Keywords: fibromyalgia, hypertension, sexual and erectile dysfunction, memory enhancement, relaxation and alertness, deep sleep, allergies, asthma

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.

This eight-week clinical study was a double-blind, placebo-controlled study using ECE as an adjunct therapy to the FM patients' current standard of physician care. The trial was conducted to establish safety of ECE with FM patients as well as initial indications of efficacy on both a single dose and high dose. Standard FM clinical trial assessment forms typically found in FM clinical trials were used, together with physician visits to monitor for toxicity, adverse events, as well as performance of blood tests and EKGs. Aside from the discontinuation of the study by six patients who had pre-existing diarrhea form of IBS, the results established the general safety of ECE. Preliminary efficacy measures showed statistically significant changes in the following:

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).

Figure 1: Hours Slept Each Night Before and After Therapy

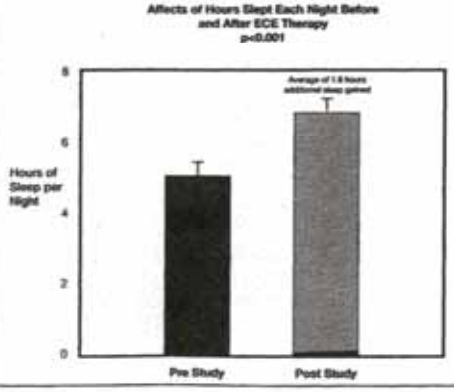


Figure 2: Quality of Sleep

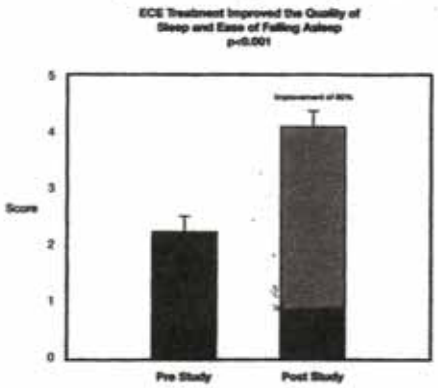


Figure 3: Reduction in Overall Fatigue

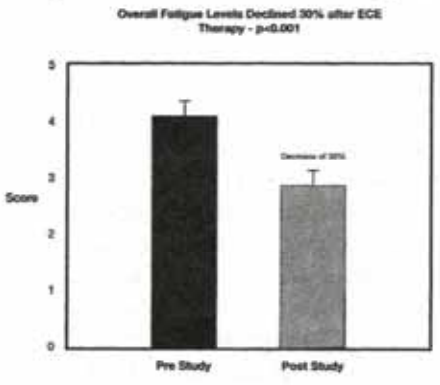


Figure 4: Summary Data for Pain Inventory

---MEAN OF MEANS---

QUESTION USED IN ANALYSIS	MEAN OF MEANS		SIGNIFICANCE P value
	T0	T8	
All questions in inventory	6.97	4.84	P<0.001 Very significant

The Molecular Structure of ECE Compared with other Polyphenols

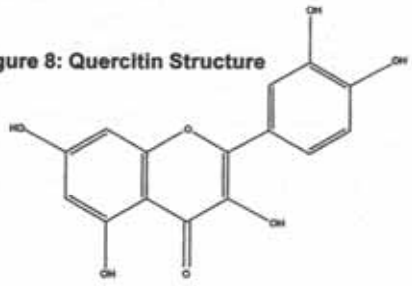
Resveratrol

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.

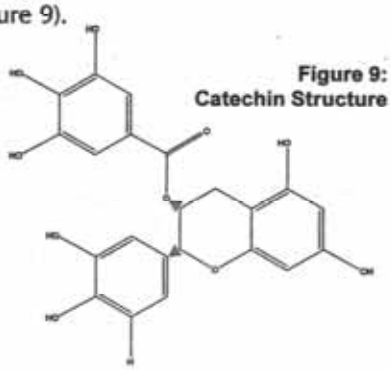
Figure 8: Quercitin Structure



Green Tea Catechins

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

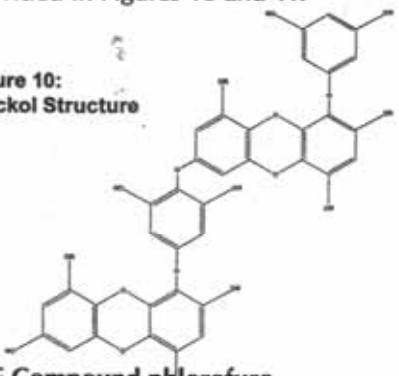
Figure 9: Catechin Structure



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.

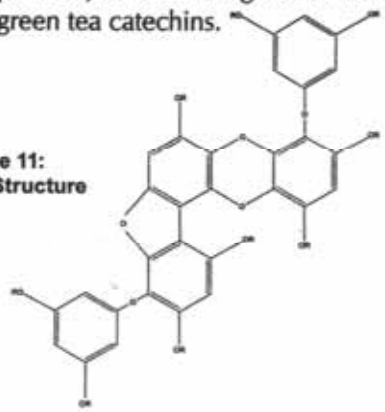
Figure 10: Dieckol Structure



ECE Compound phlorofuro-fucoeckol (PFF)

The ECE compound phlorofuro-fucoeckol (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 5: Pain Inventory

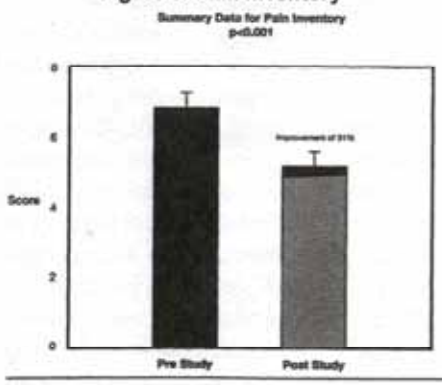


Figure 6: Number of Good Days

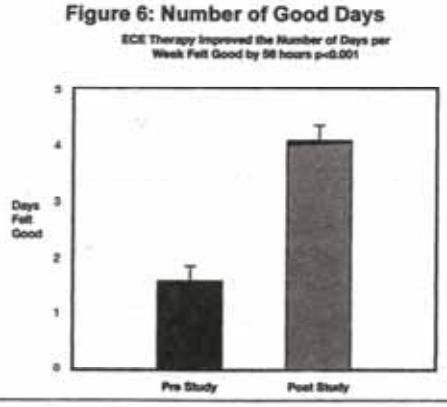
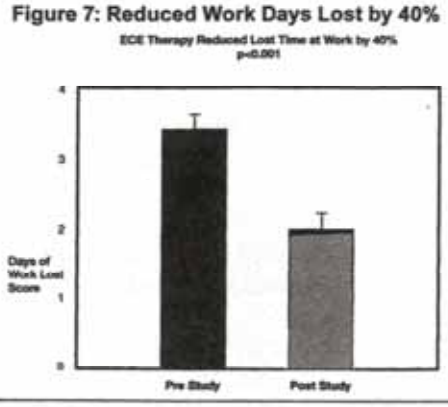


Figure 7: Reduced Work Days Lost by 40%



➤

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 200mmg/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

- Uniquely strong antioxidant scavenging of lipids, calcium, iron, and cholesterol as well as "free radicals" from the cardiovascular system (thereby lowering risk of stroke and cardiovascular events, lowering cholesterol levels, and reducing vasculitis-associated neuropathy)
- Strong anti-plasmin inhibition effect (i.e., enhances blood flow, thereby lowering blood pressure and increasing arterial blood flow)
- 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

Chapman VJ, Chapman DJ. *Seaweeds and Their Uses*. London: Chapman & Hall; 1980.

Glombitza KW, Gerstberger G. Phlorotannins with dibenzodioxin structural elements from the brown alga eisenia arborea. *Phytochemistry*. 1985;24: 543-551.

Hoppe HA. Marine algae and their products and constituents in pharmacy. In: *Marine Algae in Pharmaceutical Science*. Hoppe HA, Levring T, Tanaka Y, eds. Berlin & New York: Walter de Gruyter; 1979.

Antioxidant Function

Athukorala Y, Kim KN, Jeon YJ. Antiproliferative and antioxidant properties of an enzymatic hydrolysate from brown alga, Ecklonia cava. *Food Chem Toxicol*. 2006 Jul;44(7):1065-74. Epub 2006 Mar 3.

Kang KA, Lee KH, Chae S, Zhang R, Jung MS, Ham YM, Baik JS, Lee NH, Hyun JW. Cytoprotective effect of phloroglucinol on oxidative stress induced cell damage via catalase activation. *J Cell Biochem*. 2006 Feb 15;97(3):609-20.

Kang KA, Lee KH, Chae S, Zhang R, Jung MS, Lee Y, Kim SY, Kim HS, Joo HG, Park JW, Ham YM, Lee NH, Hyun JW. Eckol isolated from Ecklonia cava attenuates oxidative stress induced cell damage in lung fibroblast cells. *FEBS Lett*. 2005 Nov 21;579(28):6295-304. Epub 2005 Oct 19.

Kang KA, Zhang R, Lee KH, Chae S, Kim BJ, Kwak YS, Park JW, Lee NH, Hyun JW. Protective effect of triphlorethol-A from Ecklonia cava against ionizing radiation *in vitro*. *J Radiat Res* (Tokyo). 2006 Mar;47(1):61-8.

Kang K, Park Y, Hwang HJ, Kim SH, Lee JG, Shin HC. Antioxidative properties of brown algae polyphenolics and their perspectives as chemopreventive agents against vascular risk factors. *Arch. Pharm. Res*. 2003;26: 286-293.

Kang KJ, Hwang HJ, Hong DH, Park YJ, Kim SH, Lee BH, Shin HC. "Anti-Oxidant and Anti-Inflammatory Activities of Ventol, A Phlorotannin-Rich Natural Agent Derived From Ecklonia Cava, and Its Effect on Proteoglycan Degradation in Cartilage Explant Culture." Submitted to *Molecular Pathology And Pharmacology*.

Nakamura T, Nagayama K, Uchida K, Tanaka R. Antioxidant activity of phlorotannins isolated from the brown alga eisenia bicyclis. *Fisheries Sci*. 1996;62: 923-926.

Allergies/Asthma

Aikawa T, Shimura S, Sasaki H, Ebina M, Takishima T. Marked goblet cell hyperplasia with mucus accumulation in the airways of patients who died of severe acute asthma attack. *Chest*. 1992;101:916-921.

Djukanovic R, Wilson JW, Britten KM, Wilson SJ, Walls AF, Roche WR, Howarth PH, Holgate ST. Quantitation of mast cells and eosinophils in the bronchial mucosal of symptomatic atopic asthmatics and healthy control subjects using immunohistochemistry. *Am. Rev. Respir. Dis*. 1990;142:863-871.

Grunig G, Warnock M, Wakil AE, Venkayya R, Brombacher F, Rennick DM, Sheppard D, Mohrs M, Donaldson DD, Locksley RM, Corry DB. Requirement For Il-13 Independently Of Il-4 In Experimental Asthma. *Science*. 1998;282:2261-2263.

Henderson WR, Chi EY. Ultrastructural characterization and morphometric analysis of human eosinophil degranulation. *J. Cell Sci*. 1985;73:33-48.

➤

Ecklonia Cava Extract

➤

Henderson WR, Jr., Lewis DB, Albert RK, Zhang Y, Lamm WJE, Chiang GKS, Jones F, Eriksen P, Tien Y, Jonas M, Chi EY. The importance of leukotrienes in airway inflammation in a mouse model of asthma. *J. Exp. Med.* 1996;184:1483-1494.

Henderson WR, Jr., Chi EY, Maliszewski CR. Soluble interleukin-4 receptor (sil-4r) inhibits airway inflammation following allergen challenge in a mouse model of asthma. *J. Immunol.* 2000;164:1086-1095.

Hoshino M, Nakamura Y, Sim JJ. Expression of growth factors and remodeling of the airway wall in bronchial asthma. *Thorax.* 1998;53:21-27.

Kang KA, Lee KH, Chae S, Koh YS, Yoo BS, Kim JH, Ham YM, Baik JS, Lee NH, Hyun JW. Triphlorethol-A from Ecklonia cava protects V79-4 lung fibroblast against hydrogen peroxide induced cell damage. *Free Radic Res.* 2005 Aug;39(8):883-92.

Kang KA, Lee KH, Chae S, Zhang R, Jung MS, Lee Y, Kim SY, Kim HS, Joo HG, Park JW, Ham YM, Lee NH, Hyun JW. Eckol isolated from Ecklonia cava attenuates oxidative stress induced cell damage in lung fibroblast cells. *FEBS Lett.* 2005 Nov 21;579(28):6295-304. Epub 2005 Oct 19.

Krug N, Madden J, Redington AE, Lackie P, Djukanovic R, Schauer U, Holgate ST, Frew AJ, Howarth PH. T-cell cytokine profile evaluated at the single cell level in bal and blood in allergic asthma. *Am. J. Respir. Cell Mol. Biol.* 1996;14:319-326.

Kay AB. T cells as orchestrators of the asthmatic response. *Ciba Found. Symp.* 1997;206:56-67.

Roche WR, Beasley R, Williams JH, Holgate ST. Subepithelial fibrosis in the bronchi of asthmatics. *Lancet.* 1989;1:520-524.

Temann UA, Prasad B, Gallup MW, Basbaum C, Ho SB, Flavell RA, Rankin JA. A novel role for murine il-4 *in vivo*: induction of muc5ac gene expression and mucin hypersecretion. *Am. J. Respir. Cell Mol. Biol.* 1997;16:471-478.

Wills-Karp MJ, Luyimbazi, Xu X, Schofield B, Neben TY, Karp CL, Donaldson DD. Interleukin-13: central mediator of allergic asthma. *Science.* 1998;282:2258-2261.

Zhu Z, Homer RJ, Wang Z, Chen Q, Geba GP, Wang J, Zhang Y, Elias JA. Pulmonary expression of interleukin-13 causes inflammation, mucus hypersecretion, subepithelial fibrosis, physiologic abnormalities, and eotaxin production. *J. Clin. Invest.* 1999;103:779-788.

Cardiovascular Support

"Compound For Improving Hypertension Containing Inhibitors Of Angiotensin Converting Enzyme Activity Extracted From Marin Plants And Articles Comprising Thereof." Korean Patent Application 10-2004-24347 (Livechem, Inc)

Fukuyama Y, Kodama M, Miura I, Kinzyo Z, Kido M, Mori H, Nakayama Y, Takahashi M. Structure of an anti-plasmin inhibitor, eckol, isolated from the brown alga ecklonia kurome okamura and inhibitory activities of its derivatives on plasmin inhibitors. *Chem. Pharm. Bull.* 1989;37: 349-353.

Fukuyama Y, Kodama M, Miura I, Kinzyo Z, Mori H, Nakayama Y, Takahashi M. Anti-plasmin inhibitor. vi. structure of phlorofucofuroeckol a, a novel phlorotannin with both dibenzo-1,4-dioxin and dibenzofuran elements, from ecklonia kurome okamura. *Chem. Pharm. Bull.* 1990;38: 133-135.

Uhm CS, Kim KB, Lim JH, Pee DH, Kim YH, Kim H, Eun BL, Tockgo YC. Effective treatment with fucoidin for perinatal hypoxic-ischemic encephalopathy in rats. *Neuroscience Letters.* 2003;353: 21-24.

Kang K, Park Y, Hwang HJ, Kim SH, Lee JG, Shin HC. Antioxidative properties of brown algae polyphenolics and their perspectives as chemopreventive agents against vascular risk factors. *Arch. Pharm. Res.* 2003;26: 286-293.

Ruehl ML, Orozco JA, Stoker MB, Mcdonagh PF, Coull BM, Ritter LS. Protective effects of inhibiting both blood and vascular selectins after stroke and reperfusion. *Neurol Res.* 2002 Apr;24(3):226-32.

Erectile Dysfunction

Erectile and endothelial dysfunction in type ii diabetes-a possible link. *Diabetologia.* 2001;44: 1155-1160.

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).

Dorrance AM, Lewis RW, Mills TM. Captopril treatment reverses erectile dysfunction in male stroke prone spontaneously hypertensive rats. *Int J Impot Res.* 2002 Dec;14(6):494-7.

Hamed EA, Meki AR, Gaafar AA, Hamed SA. Role of some vasoactive mediators in patients with erectile dysfunction: their relationship with angiotensin-converting enzyme and growth hormone. *Int J Impot Res.* 2003 Dec;15(6):418-25.

Virag R, Floresco J, Richard C. Impairment Of Shear-Stress-Mediated Vasodilation Of Cavernous Arteries In Erectile Dysfunction. *Int J Impot Res.* 2004 Jan;16(1):39-42.

Fibromyalgia

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

Brain Support/Memory Enhancement

"Composition for Prevention and Improvement of Dementia and Promotion of Memory, and Healthy Assistance Foodstuffs Containing the Composition." Korean Patent Application# 10-2003-88177 (Assigned To Haengwoo Lee).

Lee BH, Stein S. "Improvement of Learning Behavior of Mice by an Antiacetylcholinesterase and Neuroprotective Agent Nx42, A Laminariales-Alga Extract" Presented to the Pharm. Soc. Kor., Spring Conference (2004); Manuscript Submitted to *Korean Journal of Food Science and Technology.*

Myung CS, Shin HC, Bao HY, Yeo SJ, Lee BH, Kang JS. Improvement of memory by dieckol and phlorofucofuroeckol in ethanol-treated mice: possible involvement of the inhibition of acetylcholinesterase. *Arch Pharm Res.* 2005 Jun;28(6):691-8.

Tsukada H, Nishiyama S, Fukumoto D, Ohba H, Sato K, Kakiuchi T. Effects of acute acetylcholinesterase inhibition on the cerebral cholinergic neuronal system and cognitive function: functional imaging of the conscious monkey brain using animal pet in combination with microdialysis. *Synapse.* 2004;52:1-10.

Arthritis/Neuralgia

Kang KJ, Hwang HJ, Hong DH, Park YJ, Kim SH, Lee BH, Shin HC. Anti-oxidant and anti-inflammatory activities of ventol, a phlorotannin-rich natural agent derived from ecklonia cava, and its effect on proteoglycan degradation in cartilage explant culture. Submitted to *Molecular Pathology and Pharmacology.*

Kim MM, Ta QV, Mendis E, Rajapakse N, Jung WK, Byun HG, Jeon YJ, Kim SK. Phlorotannins in Ecklonia cava extract inhibit matrix metalloproteinase activity. *Life Sci.* 2006 Sep 5;79(15):1436-43. Epub 2006 May 7.

Lee SH, Han SB, Baik JY. The influence of vnp intake on the symptoms of osteoarthritis of the knee joint. Clinical Report by Department of Orthopedic Surgery, Anam Hospital, Korea University Medical Center.

Mcever RP. Selectins: novel receptors that mediate leukocyte adhesion during inflammation. *Thromb. Haemost.* 1991;65:223-228.

Sheehan DC, Hrapchak BB. Connective Tissue/ Muscle Fiber Stains. In *Theory And Practice Of Histotechnology.* Columbus, Ohio: Battelle Press; 1980:180-201.

Shibata T, Fujimoto K, Nagayama K, Yamaguchi K, Nakamura, T. Inhibitory activity of brown algal phlorotannins against hyaluronidase. *Int. J. Food Sci. Tech.* 2002;37: 703-709.

Shibata T, Nagayama K, Tanaka R, Yamaguchi K, Nakamura T. Inhibitory effects of brown algal phlorotannins on secretory phospholipase a2s, lipoxygenases and cycloxygenases. *J. Appl. Phycol.* 2003;15: 61-66.

Shin HC, Hwang HJ, Kang KJ, Lee BH. An antioxidative and antiinflammatory agent for potential treatment of osteoarthritis from Ecklonia cava. *Arch Pharm Res.* 2006 Feb;29(2):165-71.

Compound For Improving Neuralgia Containing Dibenzo-P-Dioxine Derivatives Extracted From Marine Plants And Articles Comprising Thereof. Korean Patent Application 10-2004-0028066 (Livechem, Inc)

Evaluation of SEANOL on the Relief Effects on Neuralgic Pain. Sep. 30, 2005 (Manufacturer's Study).

Weight Loss/DGAT Inhibition

Cases, et al. *Proc. Natl. Acad. Sci. USA.* October 1998; 95:13018-13023.

Smith SJ, Cases S, Jensen DR, et al. *Nat Genet.* 2000;25:87-90.

Immune Support

Ahn MJ, Yoon KD, Min SY, Lee JS, Kim JH, Kim TG, Kim SH, Kim NG, Huh H, Kim J. Inhibition of HIV-1 reverse transcriptase and protease by phlorotannins from the brown alga Ecklonia cava. *Biol Pharm Bull.* 2004 Apr;27(4):544-7.

Robert J. Rowen, MD is a Phi Beta Kappa graduate of Johns Hopkins University and the University of California at San Francisco School of Medicine. He is board certified in both family medicine and emergency medicine, and has served on Alaska's State Medical Board.

Dr. Rowen is known as "The Father of Medical Freedom" for pioneering the nation's first statutory protection for alternative medicine in 1990. Today, he lives in northern California where he is in private practice with his wife, Terri Su, MD.

◆