

3-tiered sustained mood state characterized by physical energy, mental acuity, and emotional well-being



Diet / Vigor Relationship

- Mediterranean diet = Improved QOL
 - Henriquez-Sanchez et al. Eur J Clin Nutr 66(3): 360-8, 2012
- Omega3s = Reduced ADHD Sx / Improved QOL (cancer)
 - Van der Meij et al. Eur J Clin Nutr 66, 399-404, 2012
- Multivitamin = Increased Attention, Mood, Vigor
 - Kennedy et al. Psychopharmacology 211:55-68, 2010
- Overall Diet Quality = Reduced Depression / Improved QOL
 - Kuczmarski et al. J Am Diet Assoc. 110(3): 383-389, 2010
- Fast Food / Commercial baked Goods = Higher Depression Risk
 - Sanchez-Vilegas et al. Public Health Nutr 15(3), 424-432, 2011
- Food restriction (lightweight athletes) = Reduced Vigor
 - Filaire et al. Int J Sports Med. Aug; 22(6): 454-9. 2001
- Bonito (tuna) Broth (EAAs) = Reduced Fatigue / Improved Vigor
 - Kuroda & Nozawa. Biomed Res 29(4), 175-179, 2008
- Positive Psychological Well-Being = longer survival (healthy/diseased)
 - Chida & Steptoe. Psychosomatic Med 70:741-756, 2008





Prevalence of Chronic Stress

- Studies show that 50-60% of all lost working days are related to stress
- Work-related stress costs the EU more than 265 billion Euros annually
- Chronic stress is a determinant of Depression, Heart Disease, Diabetes, & Syndrome X
- Stress contributes to half of all illnesses in the United States
- 70-80% of all doctor visits are for stress-related illnesses
- More than half of all deaths before age 65 result from stressful lifestyles
- Generalized anxiety disorder affects ~183 million people worldwide
- People with high anxiety are 4.5x more likely to die of a heart attack or stroke
- 80% of workers report feeling stress on the job
- 65% = American Psychological Association
- 70-80% = World Health Organization (WHO) & Centers for Disease Control (CDC)
- 90% = American Institute of Stress (AIS)

Sources: Working on Stress - European Agency for Safety and Health at Work (http://agency.osha.eu.int)

U.S. Center for Disease Control

World Health Organization; www.whmc.af.mil

2000 Gallup Poll "Attitudes in the American Workplace"





Stress-Related Conditions

Metabolic and Long-Term Health Effects of Elevated Stress (Cortisol Overexposure/Metabolic Imbalance)

- •Increased appetite, Accelerated muscle catabolism, Suppressed fat oxidation, Enhanced fat storage (Obesity 2,694)
- Elevated cholesterol and triglyceride levels; Elevated blood pressure (Heart disease 4,604)
- ·Alterations in brain neurochemistry [dopamine/serotonin/norepinephrine] (Depression/Anxiety/ADHD 22,491)
- •Physical atrophy of brain cells (Memory problems/Dementia 3,169)
- •Insulin resistance and elevated blood-sugar levels (Diabetes 1,203)
- Accelerated bone resorption (Osteoporosis 2,675)
- •Reduced levels of testosterone (Suppressed libido 1,439)
- •Suppression of immune-cell number/activity (Frequent Colds/Flu/infection; Increased Cancer risk 9,651)



Causes of "Imbalance" (Stress)

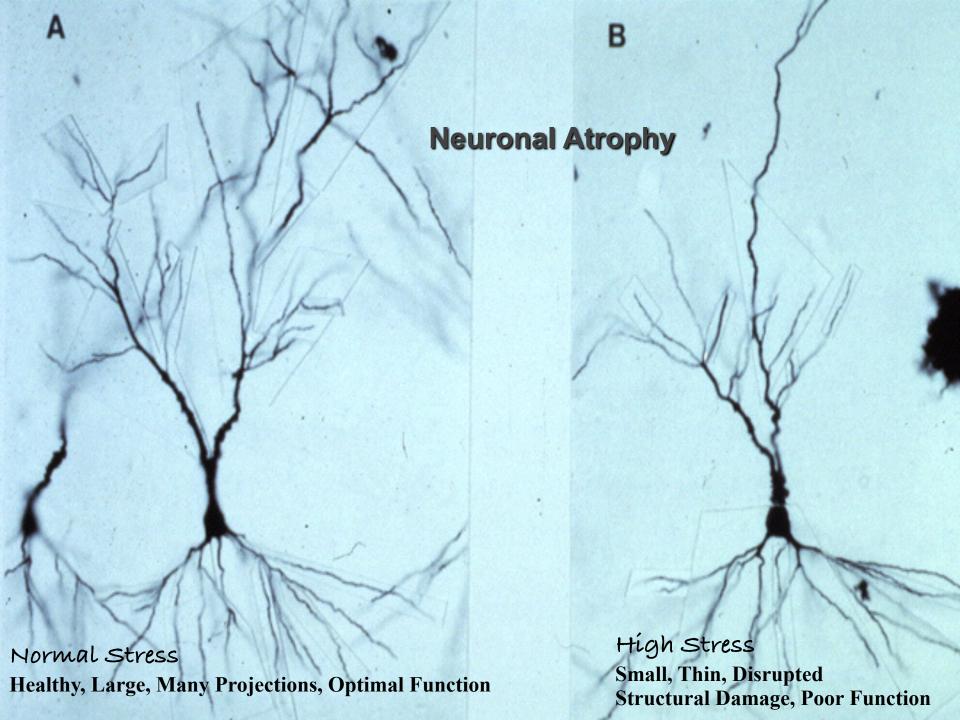
- Emotional stress (deadlines, bills, traffic...)
- Physical stress (aging, sleep deprivation, exercise...)
- Environmental stress (air/water pollution, heat, cold...)
- Non-Optimal Diet (processed foods, inadequate (phyto)nutrients...)
- Sources of Imbalance (stress) are:
 - Internal
 - External
 - Everywhere!
 - Unavoidable!!
- Athletes / Dieters / Short-Sleepers / Stressed
 - Share the SAME biochemical disruptions
 - Share the SAME psychological outcomes
 - Exhibit the SAME benefits to restored biochemical balance



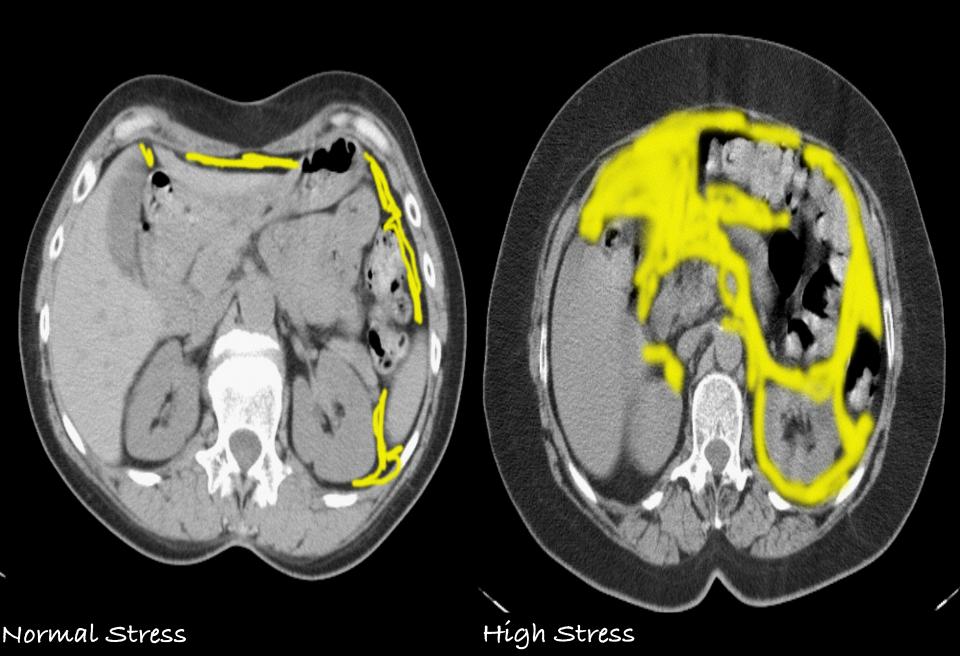








ABDOMINAL FAT ACCUMULATION



Free Radicals

- Free radicals are highly reactive, short-lived compounds that can destroy the body's fats, proteins and nucleic acids (DNA).
- Free radicals affect:
- Cardiovascular health, brain and nervous system, eye health, blood sugar and insulin metabolism, cell rejuvenation and cell protection, aging process
- Sources of free radicals
- Environmental pollution
- Radiation: UV light, X-ray, g-ray
- Smoking: 10¹⁶ free radicals/cigarette
- Normal oxidative metabolism of carbohydrates, fats & proteins for energy production.





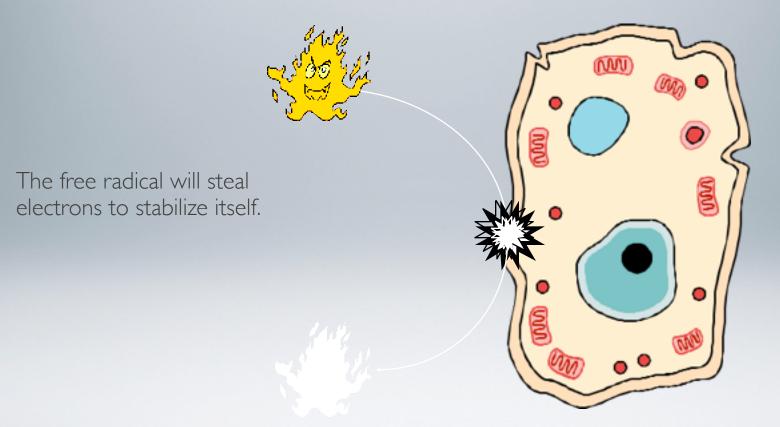
What Is a Free Radical?

A molecule or molecular fragment containing an unpaired electron in the valence orbital.





Free Radical Damage

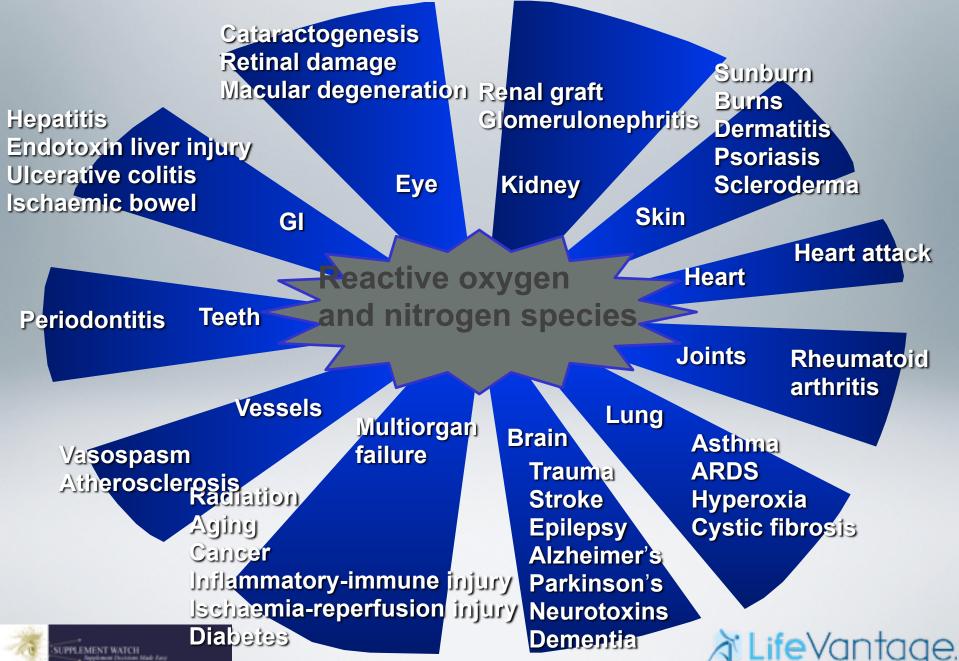


Leads to damage of lipid membranes and proteins





Clinical conditions and free radicals



Antioxidant Nutrients

- *Endogenous (enzyme) defense system
 - *Enzymes: increased with training
- *Dietary antioxidants
 - *Interact with endogenous antioxidants and form a cooperative antioxidant network
 - **Protect cell/nuclear/mitochondrial membranes from oxidative damage
- *No clear consensus whether athletes have greater needs
 - *Low fat diets, energy restriction, low fruit/vegetable intake





Endogenous Defense System

Requires co-factors for enzymes involved in antioxidant defense

- Up-regulated enzymes in athletes
- Superoxide Dismutase
- Glutathione Peroxidase
- Catalase

Copper Iron Manganese Selenium







Selected Dietary Antioxidants

Vitamin E

*Lipid soluble compound; major chain-breaking antioxidant found in cell membranes

Vitamin C







*Located in aqueous phase of cell; acts as a radical scavenger and recycles vitamin E







Selected Dietary Antioxidants

Carotenoids

- *Lipid soluble antioxidant; located in tissue membranes
 - *Examples: Yellow and Orange foods



Flavonoids

- *Antioxidants, located throughout the cell; able to scavenge radicals in lipid and aqueous phase
 - *Examples: Blue and Purple Foods





Negative Aspects of Mega-Doses

- * † tissue damage
- * oxidative stress
- *Impaired contractile function
- *Impaired performance





Antioxidants Thioredoxin_(ox) Lipid—water α-lipoic acid, NAD(P) interface glutathione disulfide Ascorbyl radical α-tocopheroxyl $NAD(P)H + H^{\dagger}$ Dihydroradical ROOH lipoic acid ROH Ascorbate (DHLA), glutathione ROO. α-tocopherol thioredoxin (red) RO. **PUFA** catechins, polyphenols O₂-• and other radicals • **Oxidants** Carotenoids Metabolism, strenuous exercise, sunlight, pollution, cigarette smoke

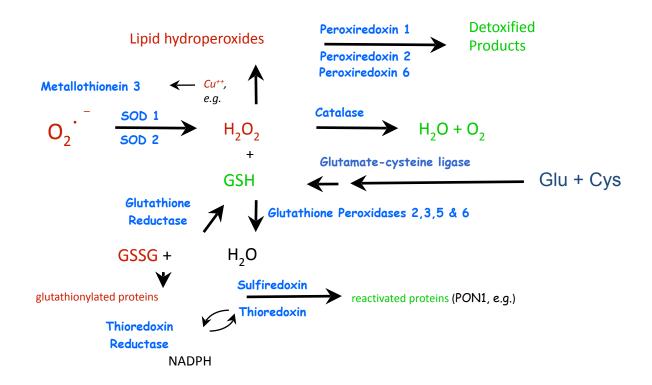








The Internal System of Protective Antioxidant Enzymes



Circulation

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Chronic Polysonary Artery Pressure Elevation Is Insufficient to Explain Right Heart Failure



ne Original Contribution

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Binata Joddar Ahr, Rashmeet K. Reen 8 Jay L. Zweier^b, Keith J. Gooch ADL®

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Associ: Protandim, a Fundamentally New Antioxidant Approach in Chemoprevention Using Mouse Two-Stage Skin Carcinogenesis as a Model

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Oxidative Stress in Mus

Warren C. McClure, MS Nicole L. Arevalo, MA Rick E. Rabon, BA Benjamin Mohr Swapan K. Bose, BS, BPharm Joe M. McCord, PhD Brian S. Tseng, MD, PhD

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Reactive Substances Predict Cardiovascular Events in Patients With Stable Coronary Artery Disease

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The Chemopreventive Effects of Protandim: Modulation of p53 Mitochondrial Translocation and Apoptosis during Skin Carcinogenesis

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Synergistic induction of heme oxygenase-1 by the components of the antioxidant supplement Protandim

Kalpana Velmurugan 45, Jawed Alam 5, Joe M. McCord 5, Subbiah Pugazhenthi 45,8

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The induction of human superoxide dismutase and catalase in vivo: A fundamentally new approach to antioxidant therapy

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Oxidative Stress in Health and Disease: The Therapeutic Potential of Nrf2 Activation

Brooks M. Hybertson, Ah Bifeng Gao, A Swapan K. Bose and Joe M. McCord Ah

*Department of Medicine, Division of Pulmonary Science and Oritical Care Medicine, University of Colorado at Denver, Aurora, CO 80045 *LifeVantage Corporation, 10613 S. Riverfront Parkway, South Jordan, UT 64095

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The Selenium and Vitamin E Cancer Prevention Trial (SELECT)

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Antioxidant Supplementation Increases the Risk of Skin Cancers in Women but Not in Men

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Annals of Internal Medicine

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The Efficacy and Safety of Multivitamin and Mineral Supplement Use To Prevent Cancer and Chronic Disease in Adults: A Systematic Review for a National Institutes of Health State-of-the-Science Conference

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See Invited Commentary and Editor's Note at end of article

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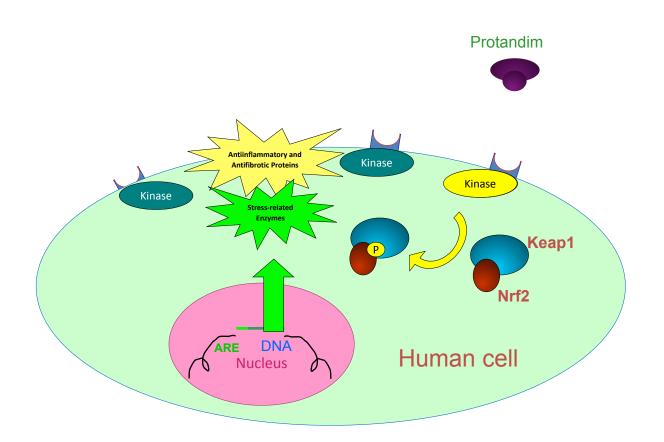
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Nrf2 = a powerful "master regulator" of antioxidant enzymes and survival genes





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Free Radical Biology & Medicine 40 (2006) 341 - 347

Original Contribution

The induction of human superoxide dismutase and catalase in vivo: A fundamentally new approach to antioxidant therapy

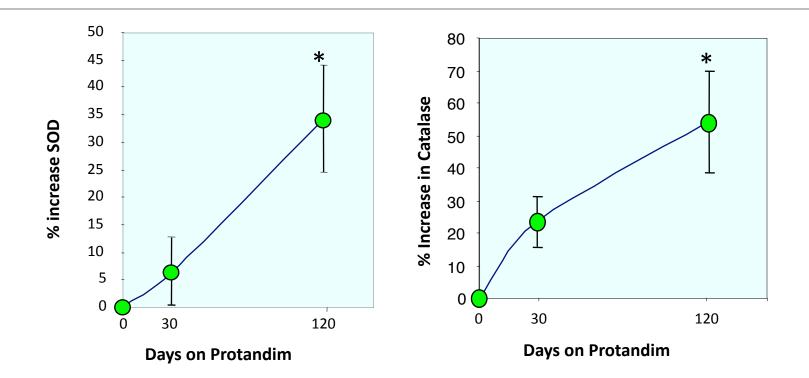
Sally K. Nelson a,b, Swapan K. Bose a, Gary K. Grunwald c, Paul Myhill d, Joe M. McCord a,b,d,*

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Abstract

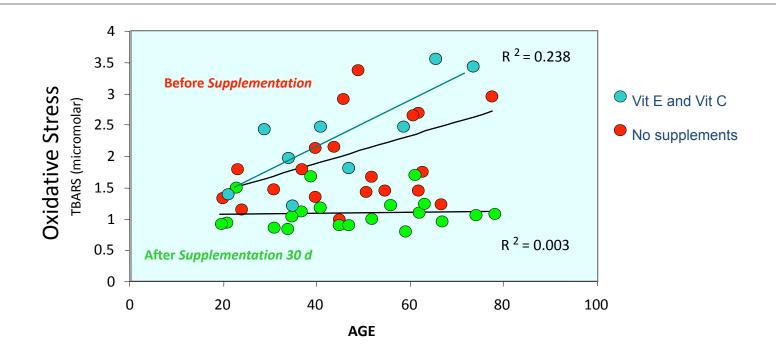
A composition consisting of extracts of five widely studied medicinal plants (Protandim) was administered to healthy human subjects ranging in age from 20 to 78 years. Individual ingredients were selected on the basis of published findings of induction of superoxide dismutase (SOD) and/or catalase in rodents in vivo, combined with evidence of decreasing lipid peroxidation. Each ingredient was present at a dosage sufficiently low to avoid any accompanying unwanted pharmacological effects. Blood was analyzed before supplementation and after 30 and 120 days of supplementation (675 mg/day). Erythrocytes were assayed for SOD and catalase, and plasma was assayed for lipid peroxidation products as thiobarbituric acid-reacting substances (TBARS), as well as uric acid, C-reactive protein, and cholesterol (total, LDL, and HDL). Before supplementation, TBARS showed a strong age-dependent increase. After 30 days of supplementation, TBARS declined by an average of 40% (p = 0.0001) and the age-dependent increase was eliminated. By 120 days, erythrocyte SOD increased by 30% (p < 0.01) and catalase by 54% (p < 0.002). We conclude that modest induction of the catalytic antioxidants SOD and catalase may be a much more effective approach than supplementation with antioxidants (such as vitamins C and E) that can, at best, stoichiometrically scavenge a very small fraction of total oxidant production.



After 120 days...

SOD increased by 34%

Catalase increased by 54%



After 30 days...

Nrf2-activation completely eliminates the age-dependent increase in lipid peroxidation

The Helping Hand



Fruits & Veggies



Lean Protein



Concentrated Carbs



Added Fat



"Healthy-Stressed" Subjects

Screened for "moderate" levels of psychological stress

- Followed for 8 weeks...
 - Stress Management
 - Exercise
 - Nutrition
 - Supplementation
 - Evaluation





Adaptogenic Supplements



- Eurycoma longifolia root extract (Eurypeptides)
- Citrus sinensis peel extract (PMFs)
- Camellia sinensis leaf extract (Catechins)
- L-Theanine (pure amino acid)
- Cordyceps sinensis mycelia extract (Cordycepic acid)
- Rhodiola rosea root extract (Rosavin)
- Eleuthercoccus senticoccus root extract (Eleutherosides)
- Withania somnifera root extract (Withanolides)
- Magnolia officinalis root extract (Honokiol)

Intended to:

- Maintain "Metabolic Balance"
 - Cortisol: Testosterone, Dopamine: Norepinephrine, Serotonin, etc...
- Deliver Healthy Energy (VIGOR)
- Enhance Mood





POMS Post-marathon

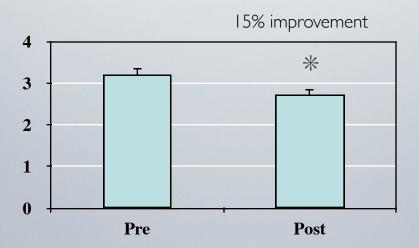
Parameter	Placebo	Recover-Ease	P value
Tension	11.5 ± 4.8	7.9±3.1	0.039
Depression	5.5 ± 7.4	2.5 ± 3.5	0.198
Anger	5.3 ± 6.1	3.4±4.2	0.377
Vigor	14.9±4.1	20.5 ± 4.8	0.005
Fatigue	9.4±5.5	4.5±2.9	0.009
Confusion	9.0 ± 3.0	6.8±1.4	0.020
Global Mood	123.5±23.0	104.4±13.0	0.015

- •Tension (-31%), Fatigue (-52%) and Confusion (-24%)
- •Vigor (+38%) and Global Mood (+16%)
- NC on measures of Depression or Anger RE = BCAA, glutamine, proteolytic enzymes, antioxidants





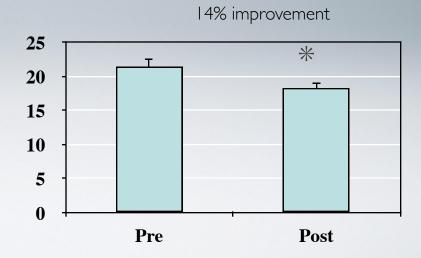
C:T Ratio (x1000)



Global Mood State (POMS)

22% improvement 180 144 108 72 36 0 Pre Post

Subjective Stress

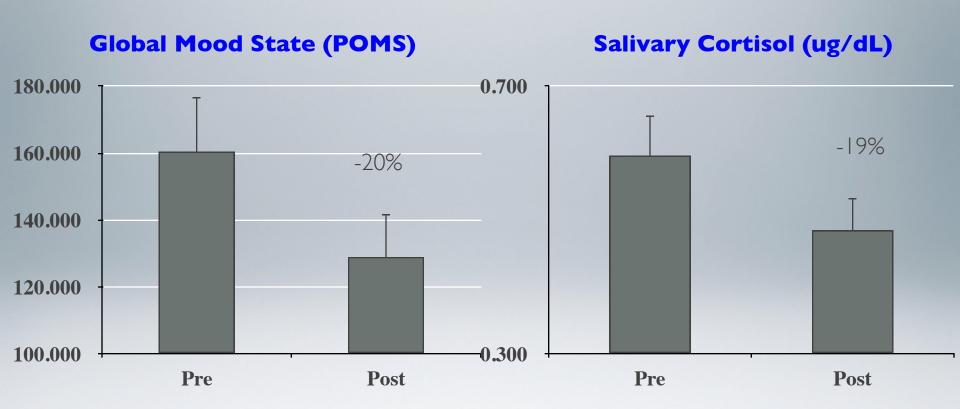






RESULTS

Global Mood State & Salivary Cortisol

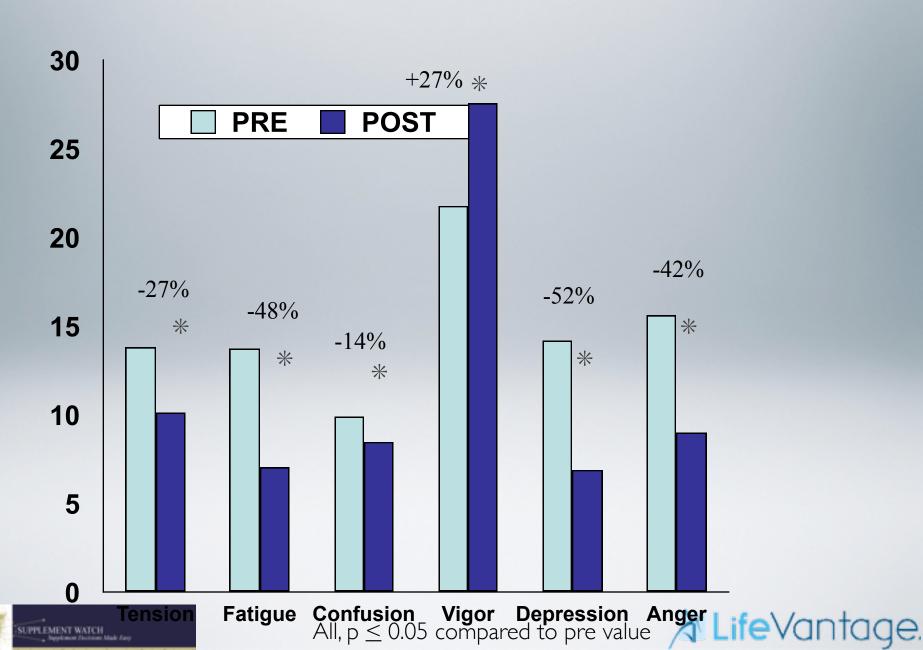


Both, $p \le 0.05$ compared to pre value





Profile of Mood States (POMS)



Dietary Supplement Combination Reduces Inflammation and Improves Mood State in Stressed Subjects



S. Talbott¹, J. Talbott¹, M. Vosti², & J. Anderson²

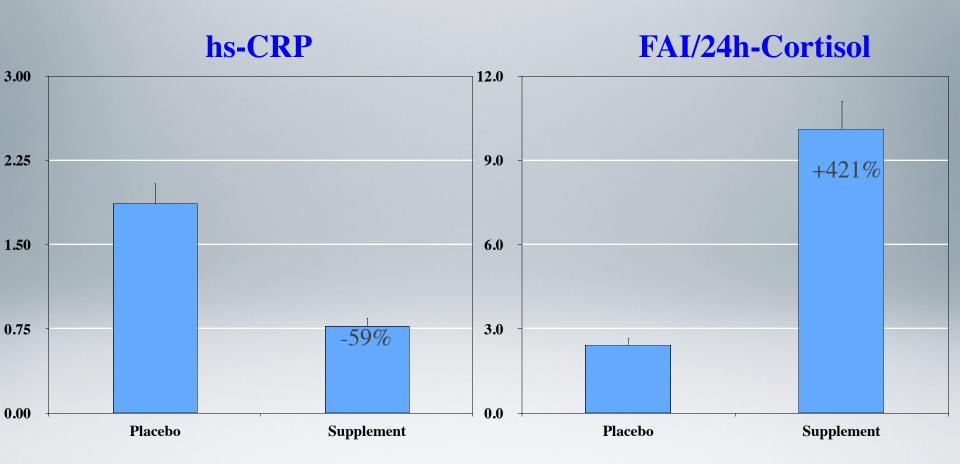
¹SupplementWatch & ²South Mountain Chiropractic, Salt Lake City (Draper), UT





RESULTS (week 4)

Inflammation & Metabolic Balance



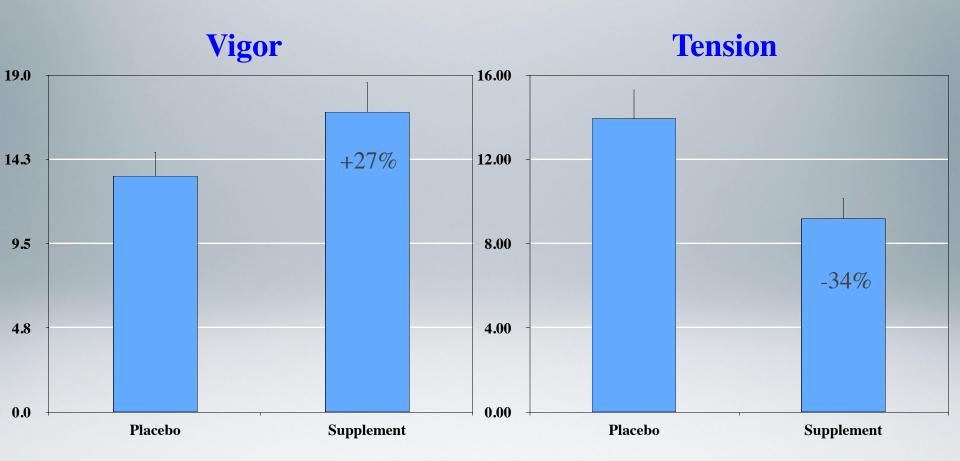
Both, $p \le 0.05$ compared to Placebo





RESULTS (week 4)

Profile of Mood States (POMS)



Both, $p \le 0.05$ compared to Placebo





Effect of Eurycoma longifolia Extract on Anabolic Balance During Endurance Exercise



S. Talbott, J. Talbott, J. Negrete, M. Nichols, and J. Roza

SupplementWatch, Inc., Salt Lake City (Draper), UT

& Source One Global, Chicago, IL



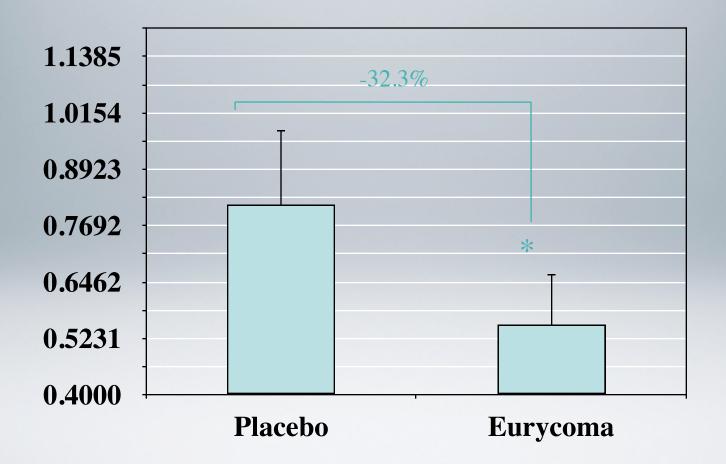






RESULTS

Salivary Cortisol (ug/dL)

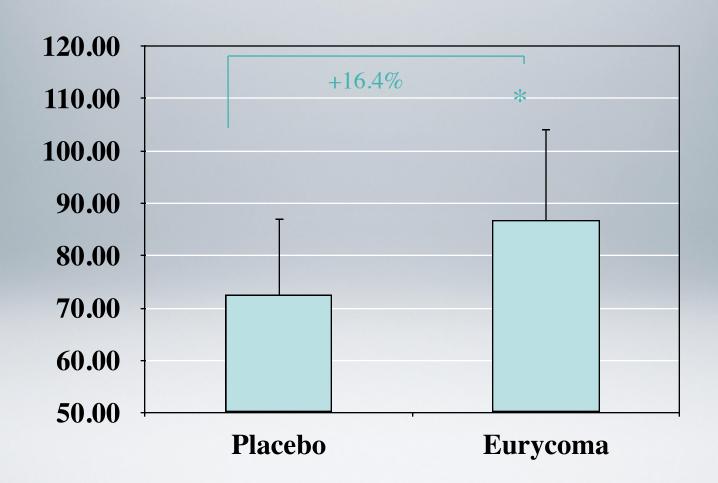






RESULTS

Salivary Testosterone (pg/dL)







Effect of Branched Chain Amino Acids on Salivary Cortisol Levels During Endurance Exercise



S. Talbott, J. Talbott, J. Negrete, and M. Nichols

SupplementWatch, Inc.

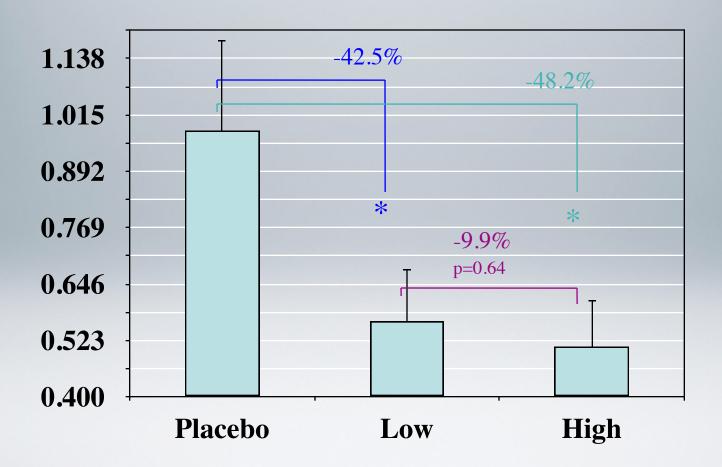
Salt Lake City (Draper), UT





RESULTS

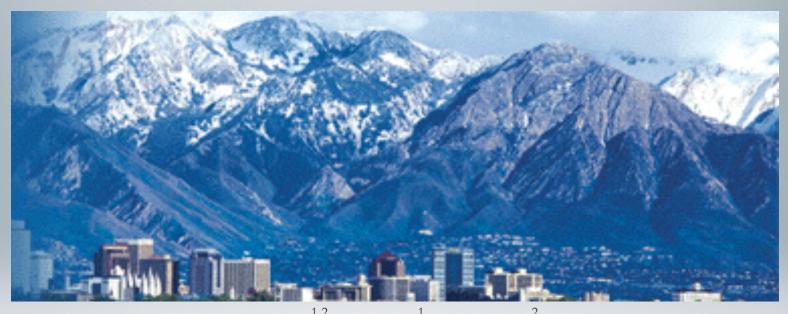
Salivary Cortisol (ug/dL)







Effect of Eurycoma longifolia and Magnolia officinalis on Hormone Balance & Mood State in Stressed Subjects



S. Talbott, J. Talbott, & M. Pugh

SupplementWatch & MonaVie, Salt Lake City, UT



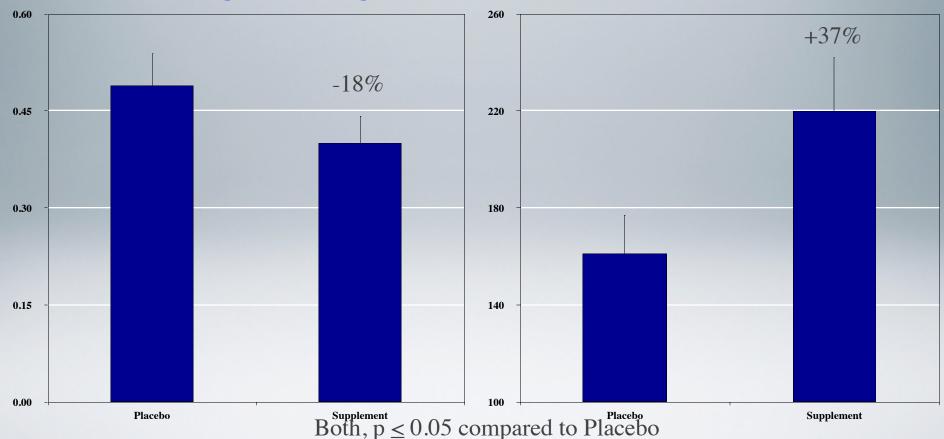


RESULTS (week 4)

Cortisol & Testosterone (% difference from Placebo)

Cortisol, ug/mL (Magnolia)

Testosterone, pg/mL (Eurycoma)



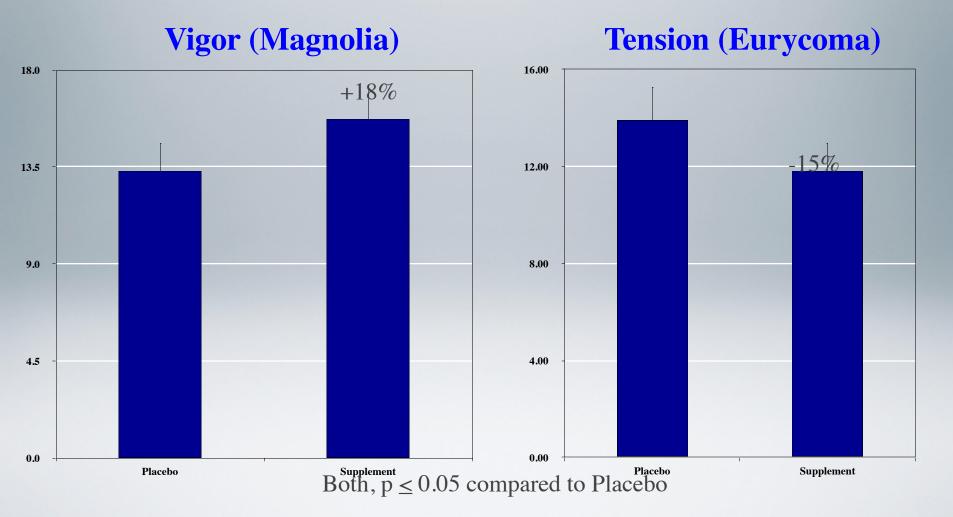






RESULTS (week 4)

Profile of Mood States (POMS)









Conclusions

- Top reasons for primary care visits involve Stress, Fatigue, Depression
- There is a strong scientific association between chronic metabolic imbalance & stress-related diseases (stress, oxidation, inflammation).
- Effect *magnitude* (~20% Global Mood & Vigor) is equivalent to:
 - Pharmaceutical treatment (Prozac, Zoloft, Celexa, etc)
 - CBSM (cognitive behavioral stress management)
- Biochemical Balance:
 - enhances weight loss (metabolic effect)
 - improves dietary compliance (behavioral effect)
 - enhances mood state & vigor (psychological effect)

