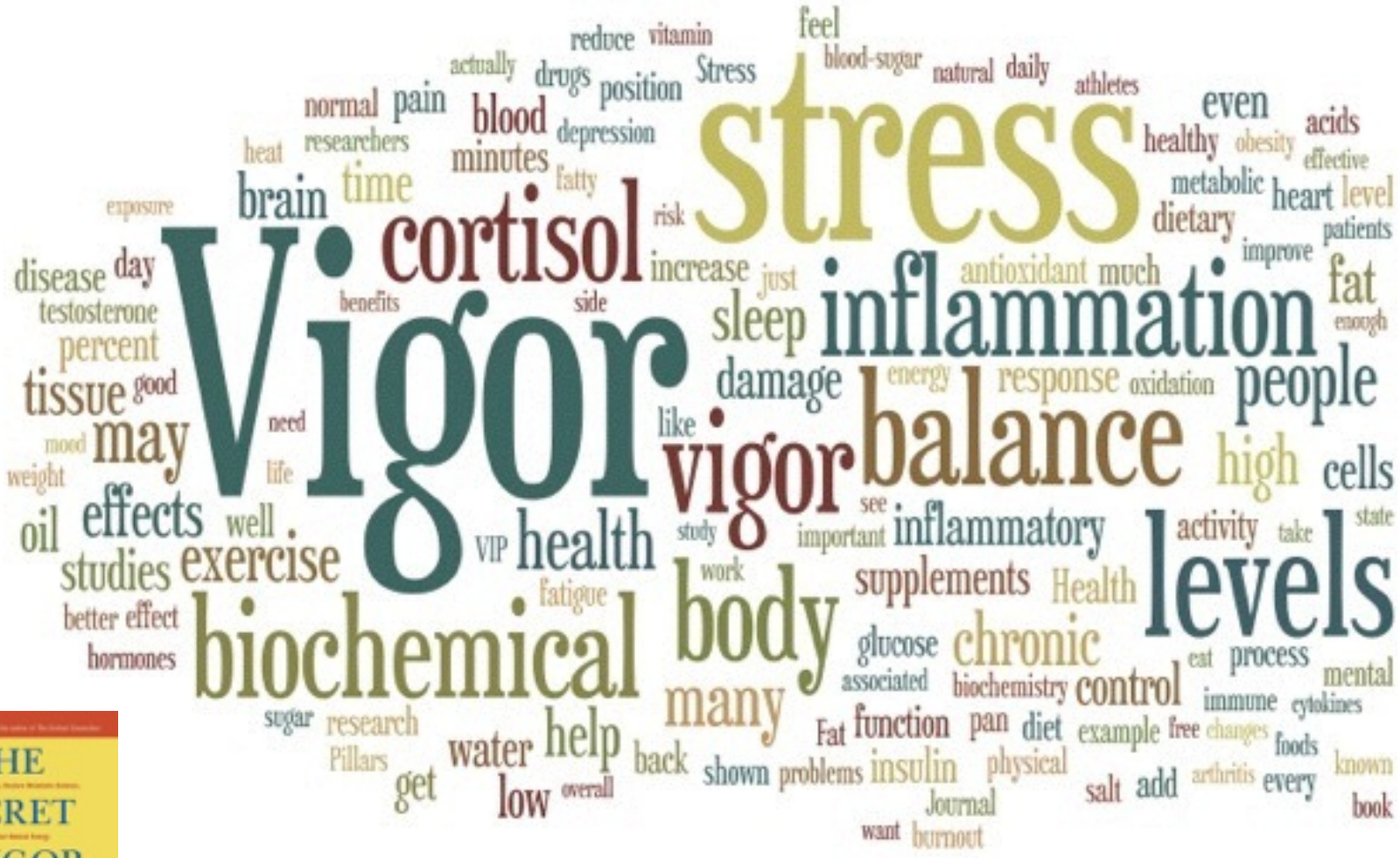
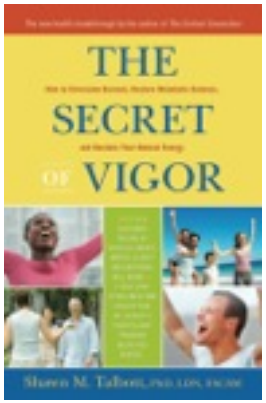




3-tiered sustained mood state characterized by physical energy, mental acuity, and emotional well-being

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)

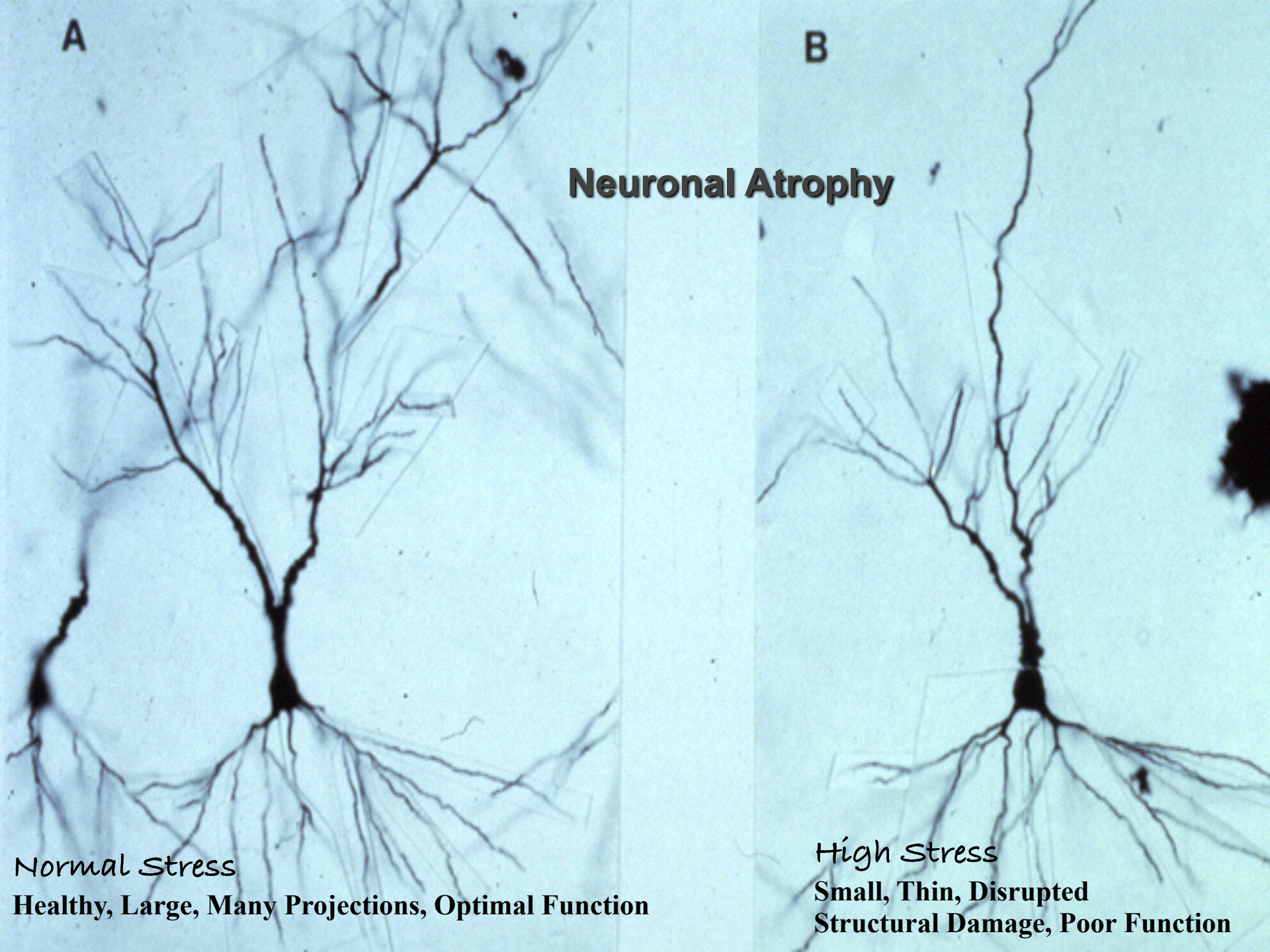
- Increased appetite, Accelerated muscle catabolism, Suppressed fat oxidation, Enhanced fat storage **(Obesity - 2,694)**
- Elevated cholesterol and triglyceride levels; Elevated blood pressure **(Heart disease - 4,604)**
- Alterations in brain neurochemistry [dopamine/serotonin/norepinephrine] **(Depression/Anxiety/ADHD - 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*


ADDERALL XR
PROZAC
PROVIGIL
(MODAFINIL)
STARBUCKS COFFEE
Lexapro
Folgers
MONSTER ENERGY
Ritalin-SR
Celexa
Vyvanse
$100B+
Wellbutrin XL
strattera
atomoxetine HCl
AMBIEN
ROCKSTAR ENERGY DRINK
EFFEXOR XR
CONCERTA
Luvox
Cymbalta
Peets Coffee & Tea
DUNKIN' DONUTS

Neuronal Atrophy



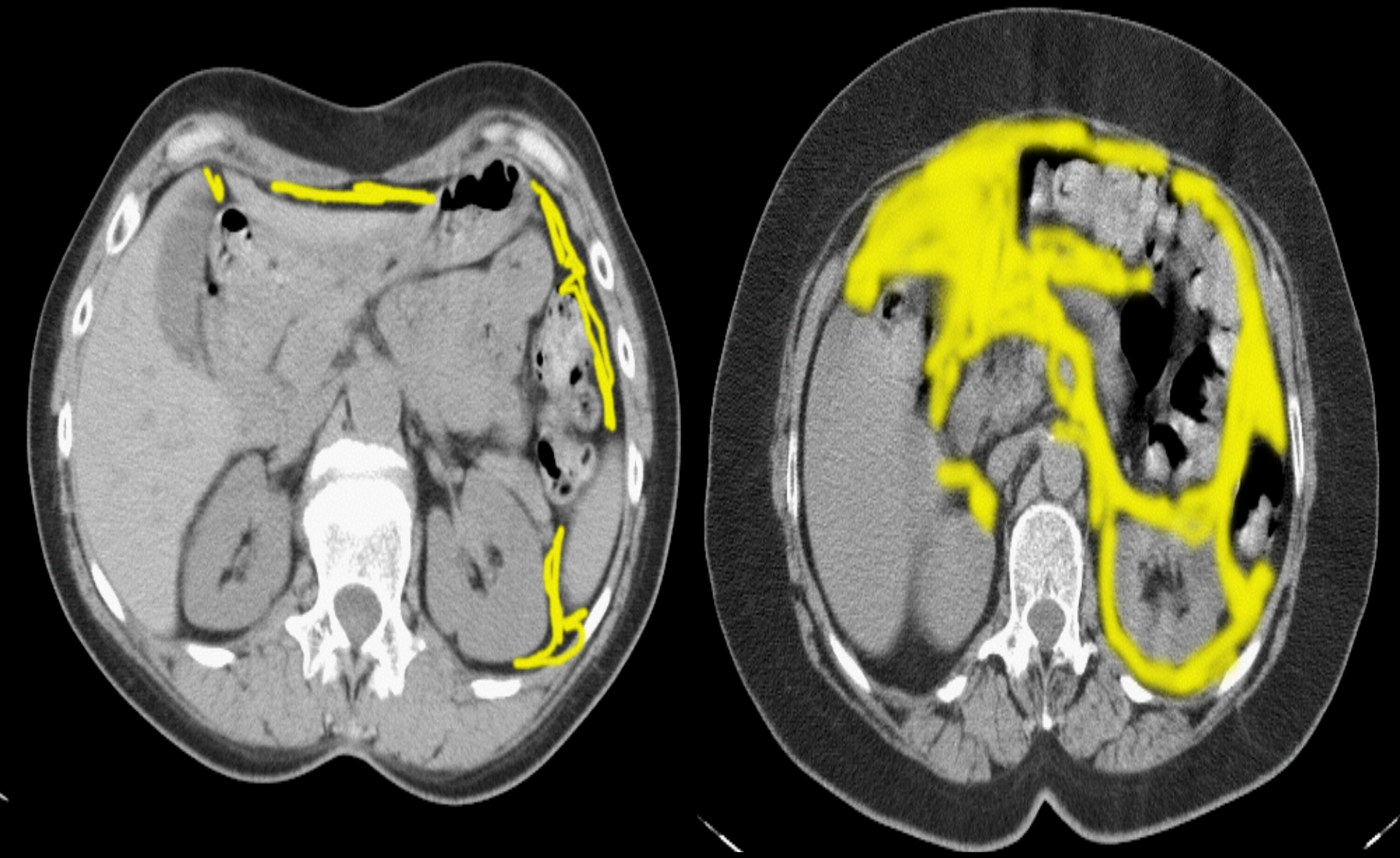
Normal Stress

Healthy, Large, Many Projections, Optimal Function

High Stress

Small, Thin, Disrupted
Structural Damage, Poor Function

ABDOMINAL FAT ACCUMULATION



Normal Stress

High Stress

Free Radicals

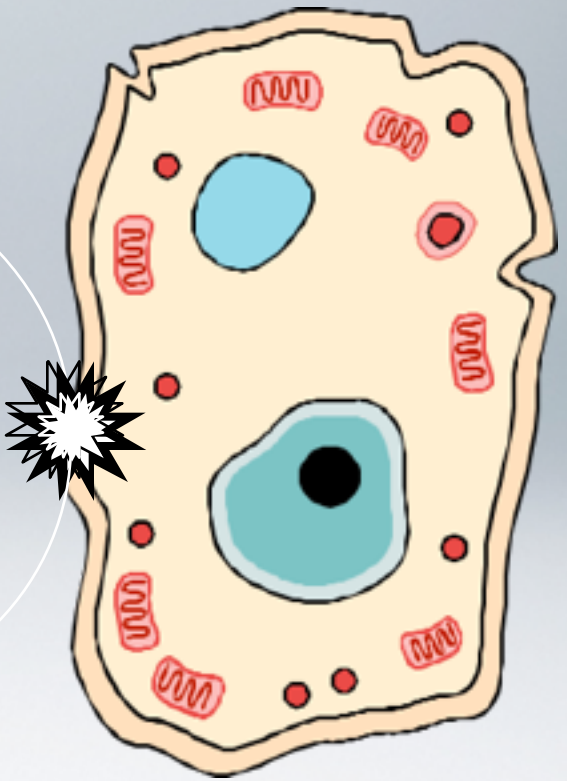
- **Free radicals are highly reactive, short-lived compounds that can destroy the body's fats, proteins and nucleic acids (DNA).**
- **Free radicals affect:**
  - Cardiovascular health, brain and nervous system, eye health, blood sugar and insulin metabolism, cell rejuvenation and cell protection, aging process
- **Sources of free radicals**
  - Environmental pollution
  - Radiation: UV light, X-ray, g-ray
  - Smoking: 10^{16} 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.

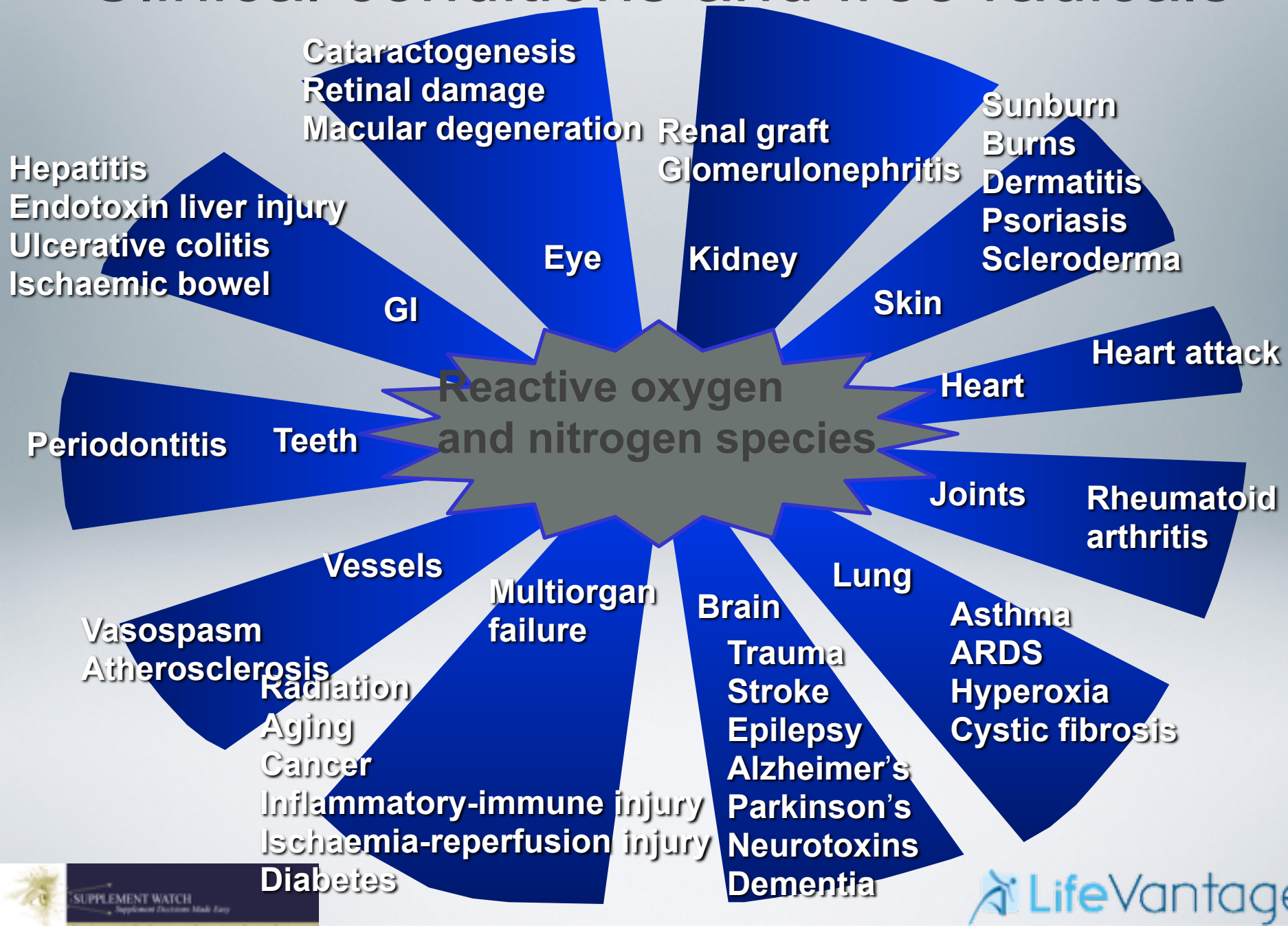
Free Radical Damage

The free radical will steal electrons to stabilize itself.



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
Zinc

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

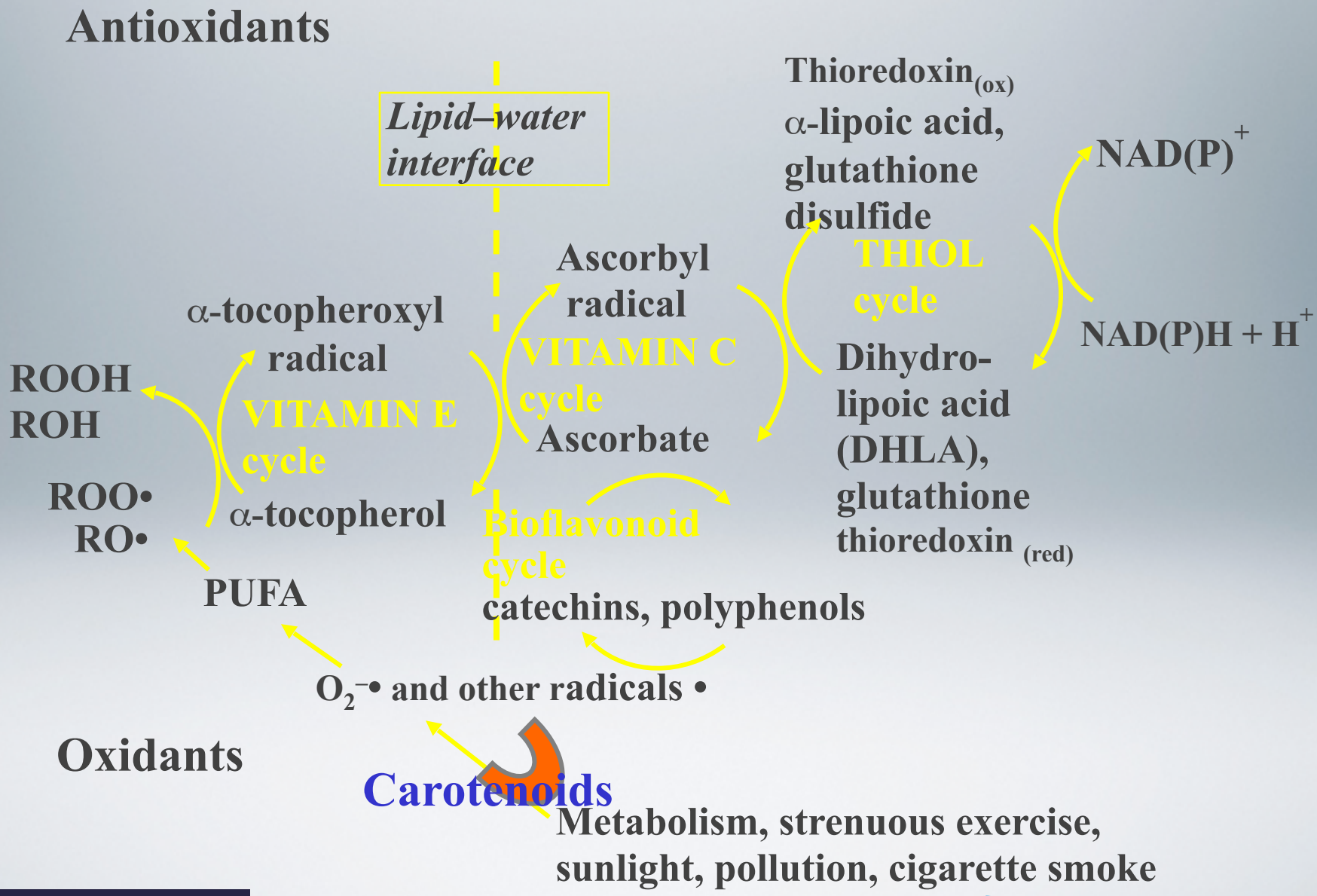
Selected Dietary Antioxidants

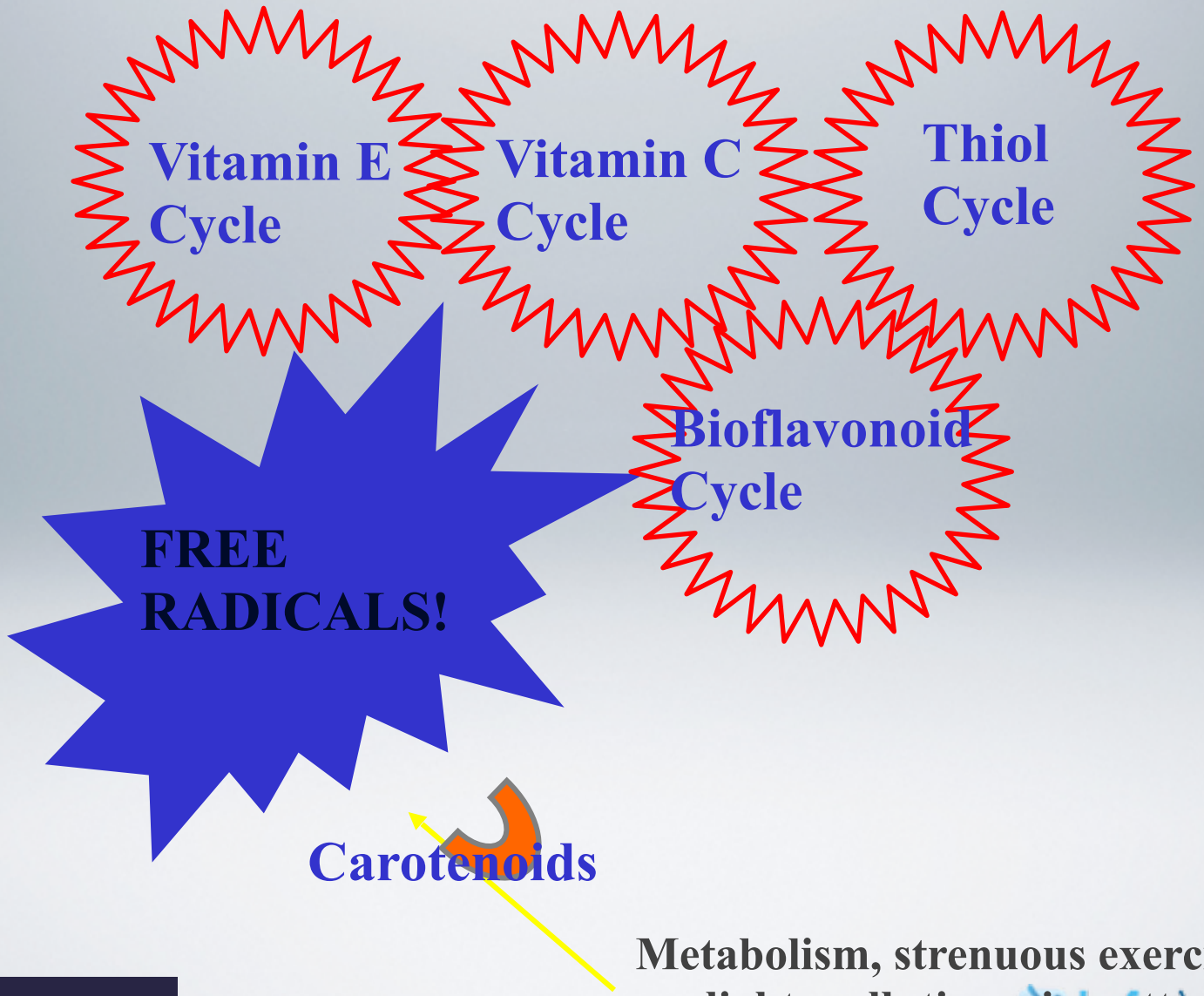
- Carotenoids
  - Lipid soluble antioxidant; located in tissue membranes
    - Examples: Yellow and Orange foods

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

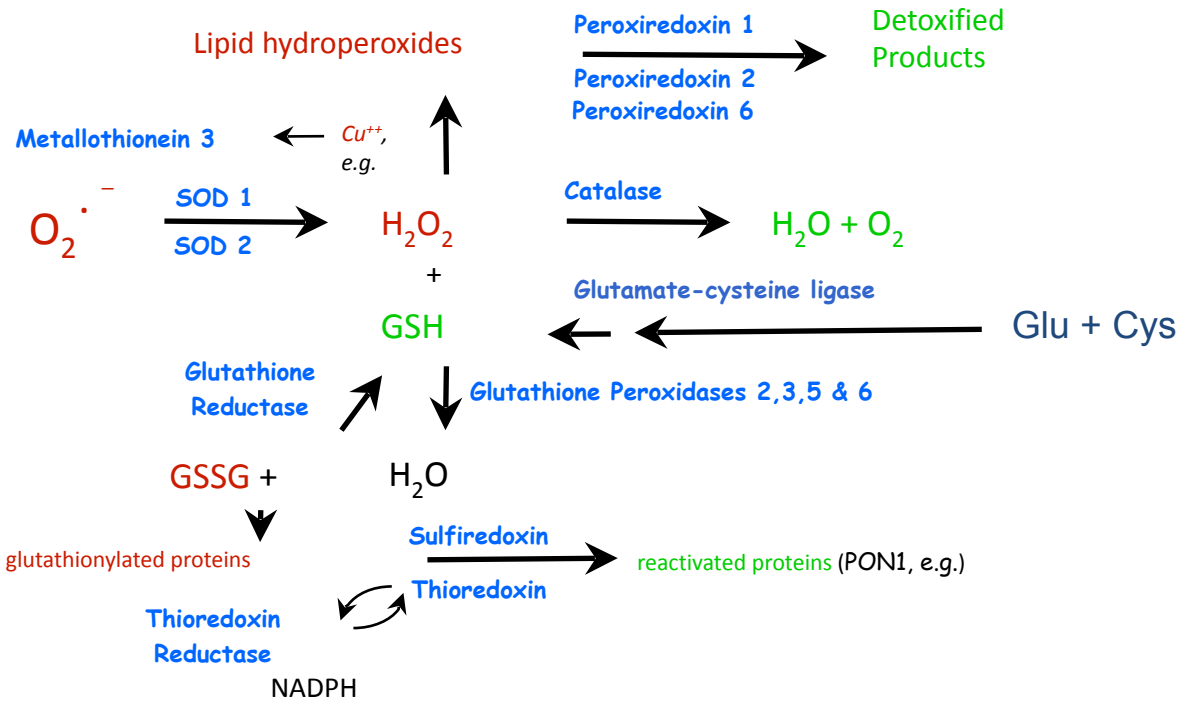
Negative Aspects of Mega-Doses

- ↑ tissue damage
- ↑ oxidative stress
- Impaired contractile function
- Impaired performance




Vitamin E Cycle
Vitamin C Cycle
Thiol Cycle
Bioflavonoid Cycle
FREE RADICALS!
Carotenoids
Metabolism, strenuous exercise, sunlight, pollution, cigarette smoke

The Internal System of Protective Antioxidant Enzymes



Circulation

Journal of the American Heart Association

Heart Failure

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

PLoS one

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

Free Radical Biology & Medicine

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

Original Contribution

Protandim attenuates intimal ex vivo via a catalase-depend

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

The Dietary Supplement Plasma Osteopontin a Oxidative Stress in Mus

Serum Levels of Thiobarbituric Acid Reactive Substances Predict Cardiovascular Events in Patients With Stable Coronary Artery Disease

A Longitudinal Analysis of the PREVENT Study

PLoS one

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

United States Patent

Molecular Aspects of Medicine

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


ORIGINAL CONTRIBUTION

Vitamin E and the Risk of Prostate Cancer
The Selenium and Vitamin E Cancer Prevention Trial (SELECT)

EFFECTS OF A COMBINATION OF BETA CAROTENE AND VITAMIN A ON LUNG CANCER AND CARDIOVASCULAR DISEASE

α-Tocopherol and β-Carotene Supplements and Lung Cancer Incidence in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study: Effects of Base-line Characteristics and Study Compliance

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

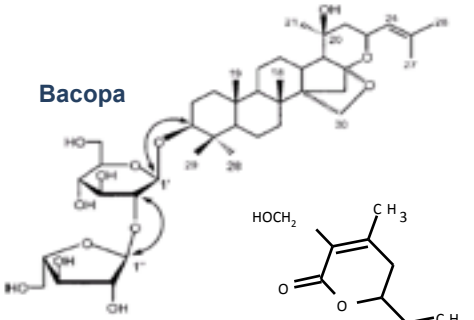
Annals of Internal Medicine — NIH CONFERENCE

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

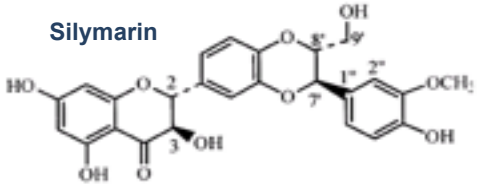
ORIGINAL INVESTIGATION

Dietary Supplements and Mortality Rate in Older Women
The Iowa Women's Health Study

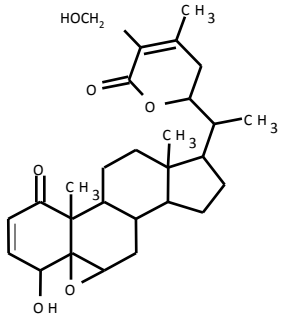
Nrf2 = a powerful "master regulator" of antioxidant enzymes and survival genes



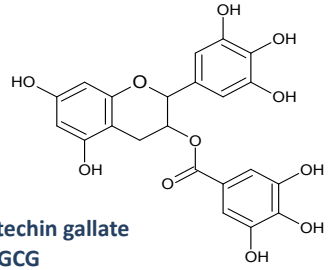
Bacopa



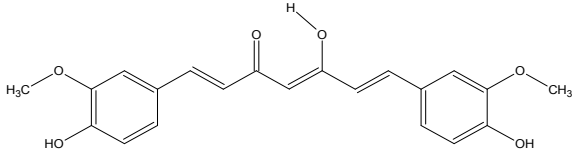
Silymarin



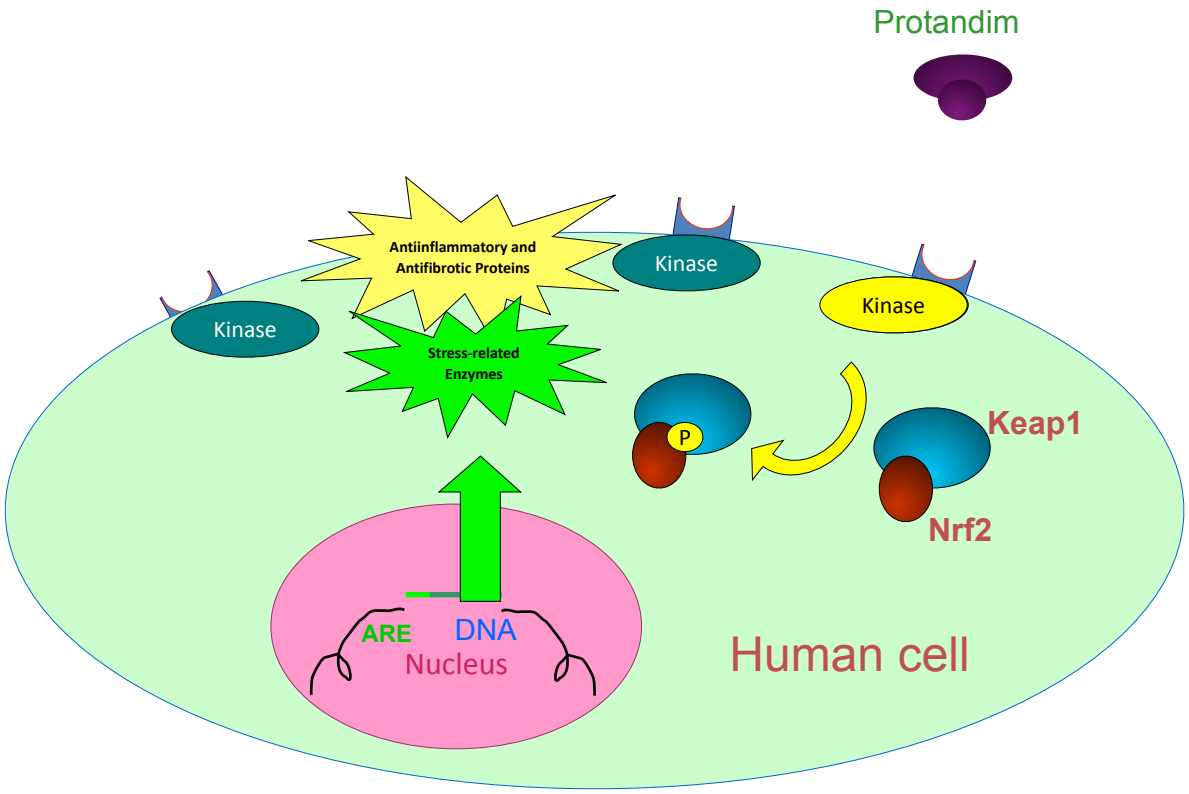
Withaferin A



Epigallocatechin gallate
EGCG



Curcumin


Protandim
Antiinflammatory and
Antifibrotic Proteins
Kinase
Kinase
Kinase
Stress-related
Enzymes
P
Keap1
Nrf2
ARE
DNA
Nucleus
Human cell

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Free Radical Biology & Medicine 40 (2006) 341 – 347
www.elsevier.com/locate/freeradbiomed

Original Contribution

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

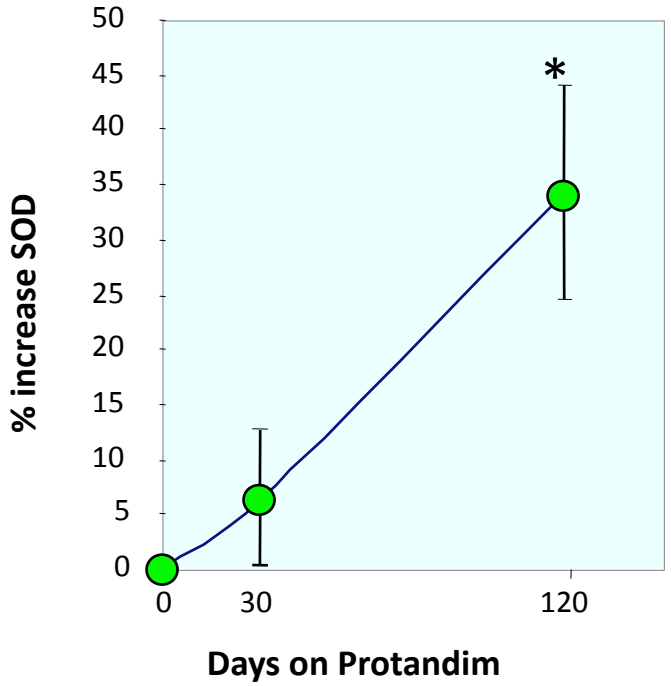
Sally K. Nelson [a,b], Swapan K. Bose [a], Gary K. Grunwald [c], Paul Myhill [d], Joe M. McCord [a,b,d,*]

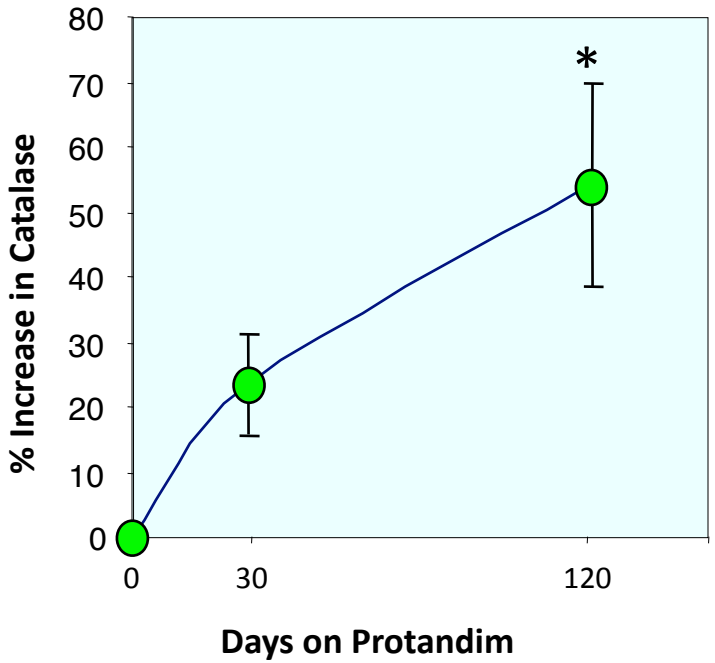
[a] Webb-Waring Institute for Cancer, Aging and Antioxidant Research, University of Colorado Denver Health Sciences Center, Denver, CO 80262, USA
[b] Department of Medicine, University of Colorado Denver Health Sciences Center, Denver, CO 80262, USA
[c] Department of Preventive Medicine and Biometrics, University of Colorado Denver Health Sciences Center, Denver, CO 80262, USA
[d] Lifeline Therapeutics, Denver, CO, USA

Received 22 June 2005; revised 24 August 2005; accepted 28 August 2005

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.

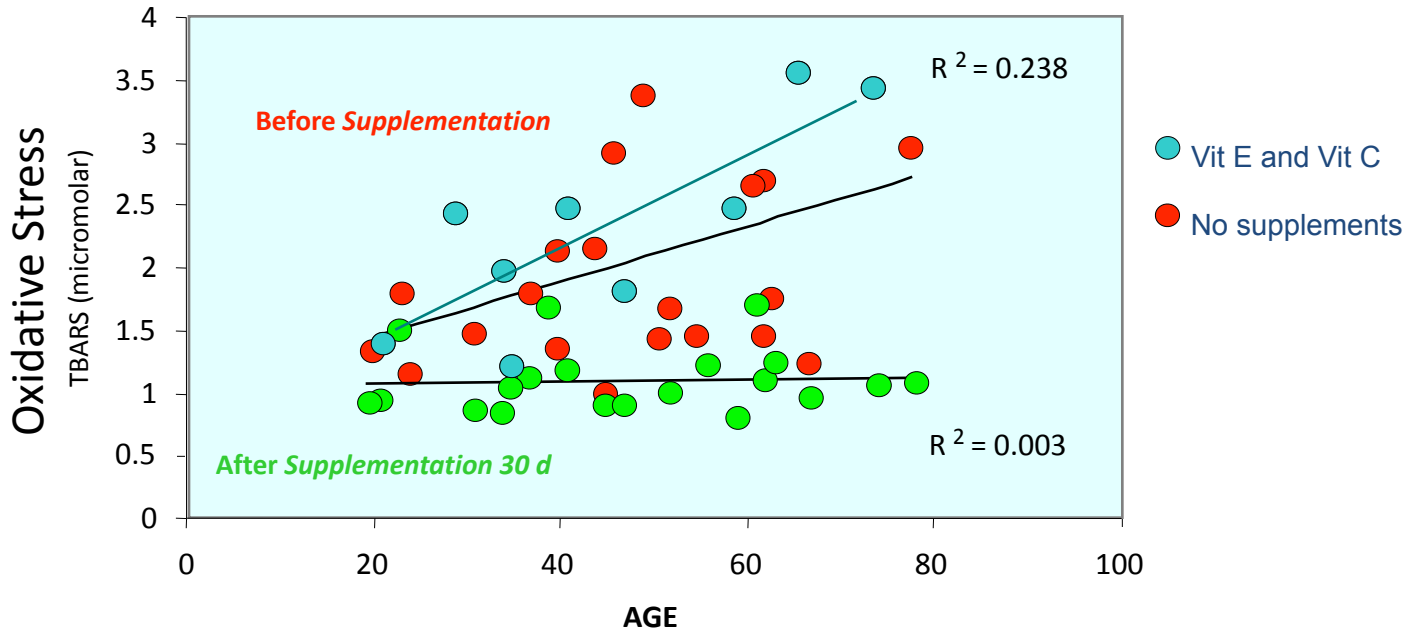




After 120 days…

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

Metabolic Controllers

"Healthy-Stressed" Subjects

Screened for "moderate" levels of psychological stress

- Followed for 8 weeks…
  - **S**tress Management
  - **E**xercise
  - **N**utrition
  - **S**upplementation
  - **E**valuation

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

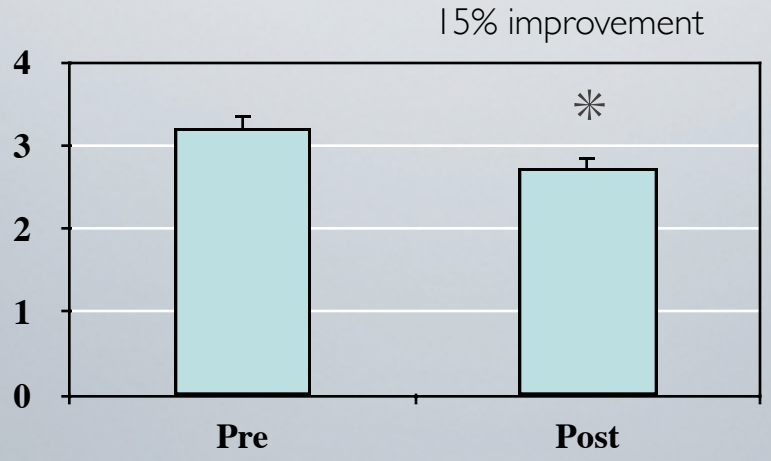
POMS Post-marathon

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

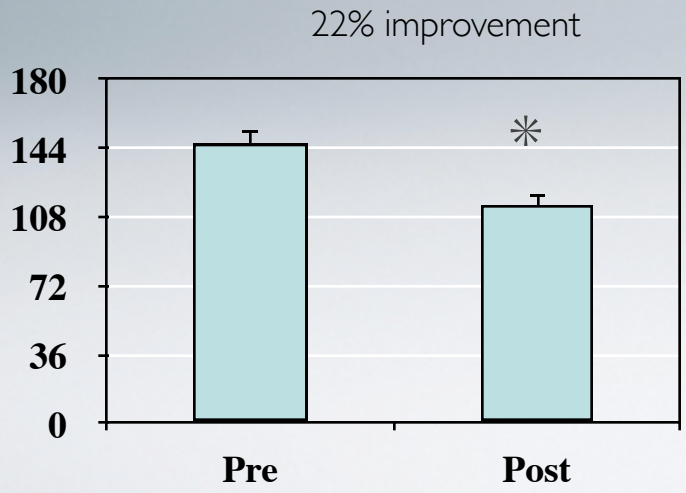
- Tension (-31%), Fatigue (-52%) and Confusion (-24%)
- Vigor (+38%) and Global Mood (+16%)
- NC on measures of Depression or Anger

RE = BCAA, glutamine, proteolytic enzymes, antioxidants

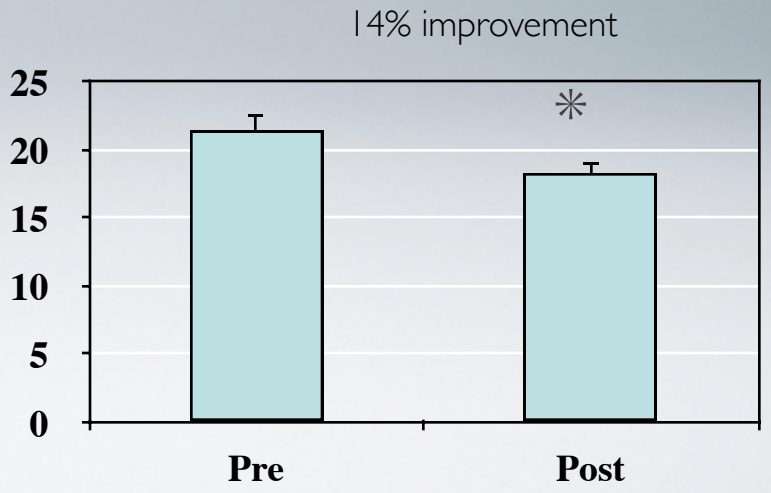
C:T Ratio (x1000)



Global Mood State (POMS)



Subjective Stress

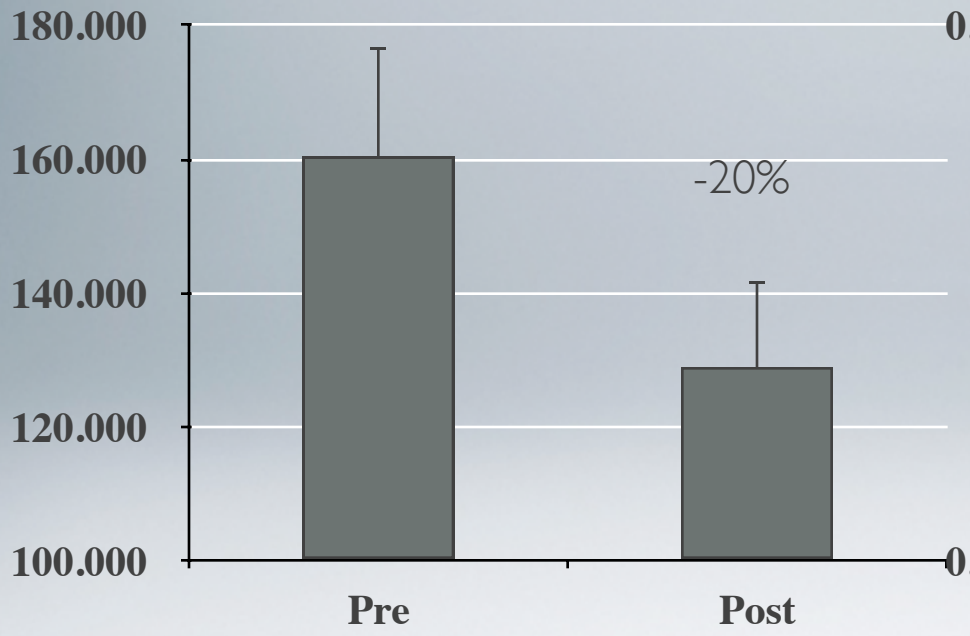


All, $p \leq 0.05$ compared to pre value

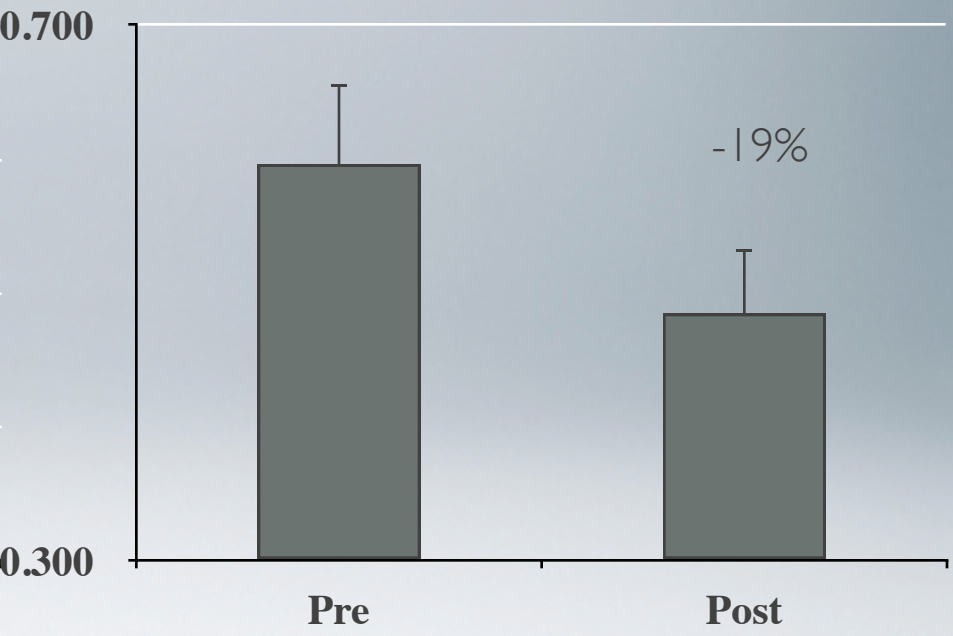
RESULTS

Global Mood State & Salivary Cortisol

Global Mood State (POMS)

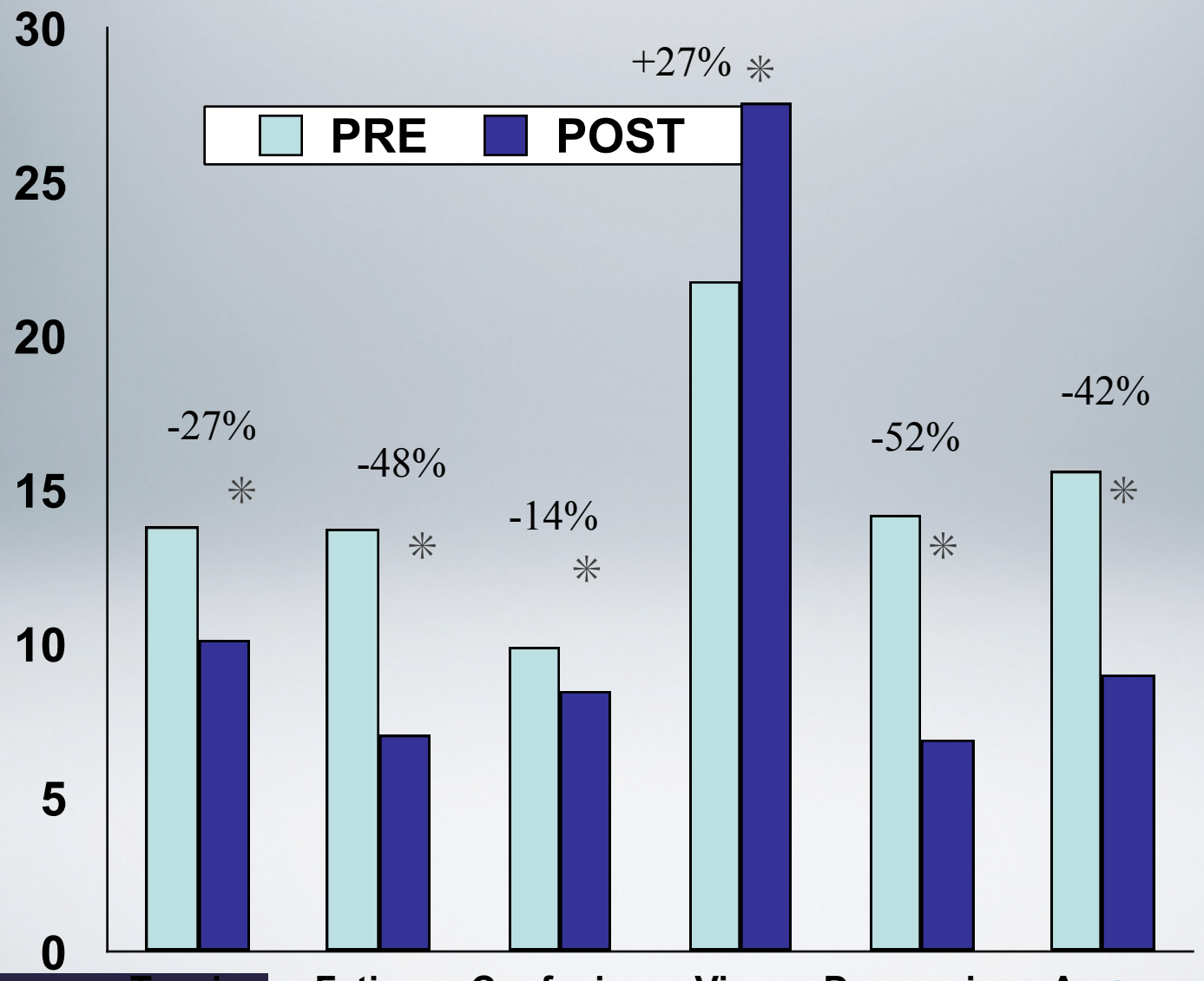


Salivary Cortisol (ug/dL)



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

Profile of Mood States (POMS)



All, $p \leq 0.05$ compared to pre value

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

S. Talbott[1], J. Talbott[1], M. Vosti[2], & J. Anderson[2]

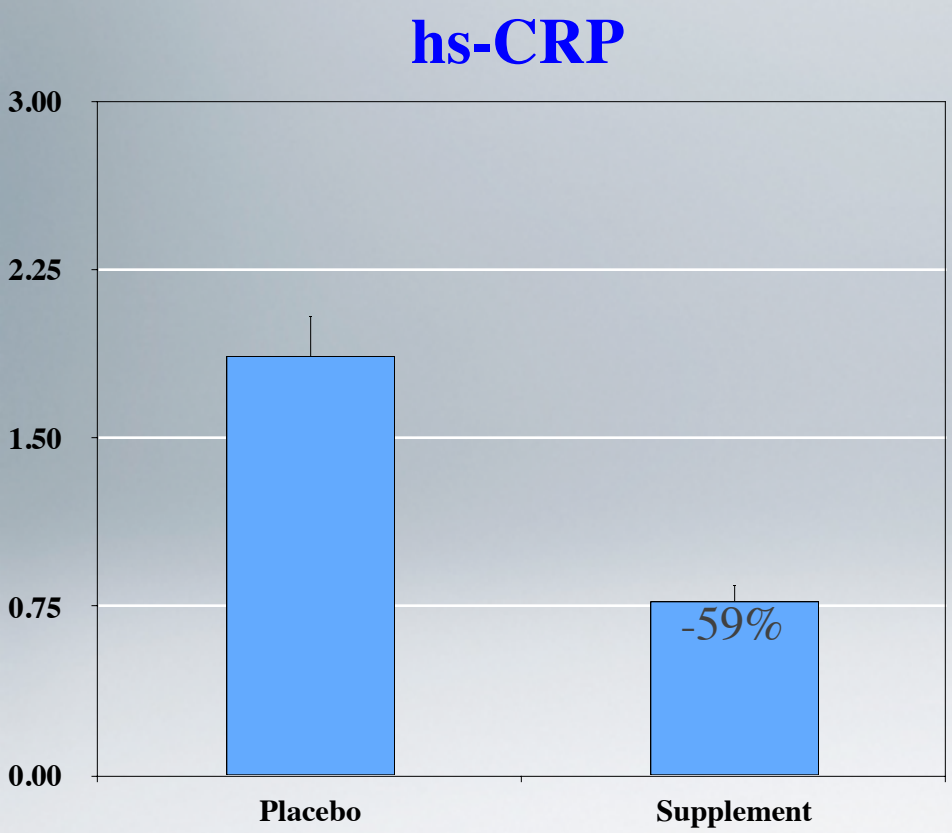
[1]SupplementWatch & [2]South Mountain Chiropractic, Salt Lake City (Draper), UT

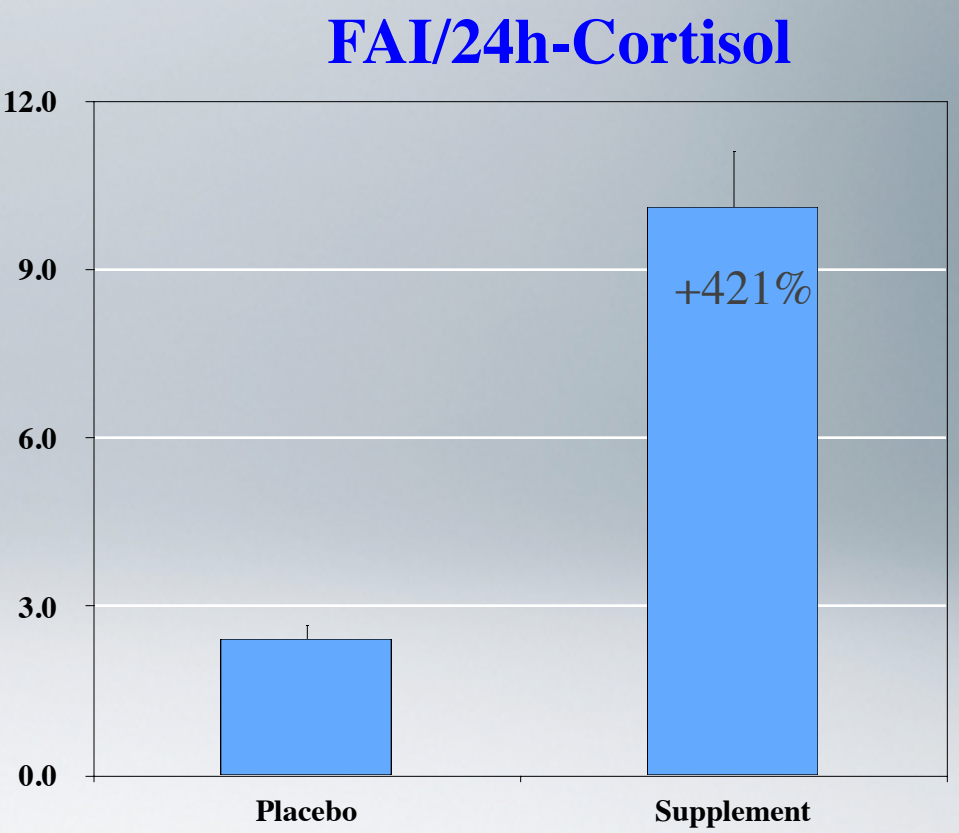
SUPPLEMENT WATCH
Supplement Decisions Made Easy

LifeVantage

RESULTS (week 4)

Inflammation & Metabolic Balance





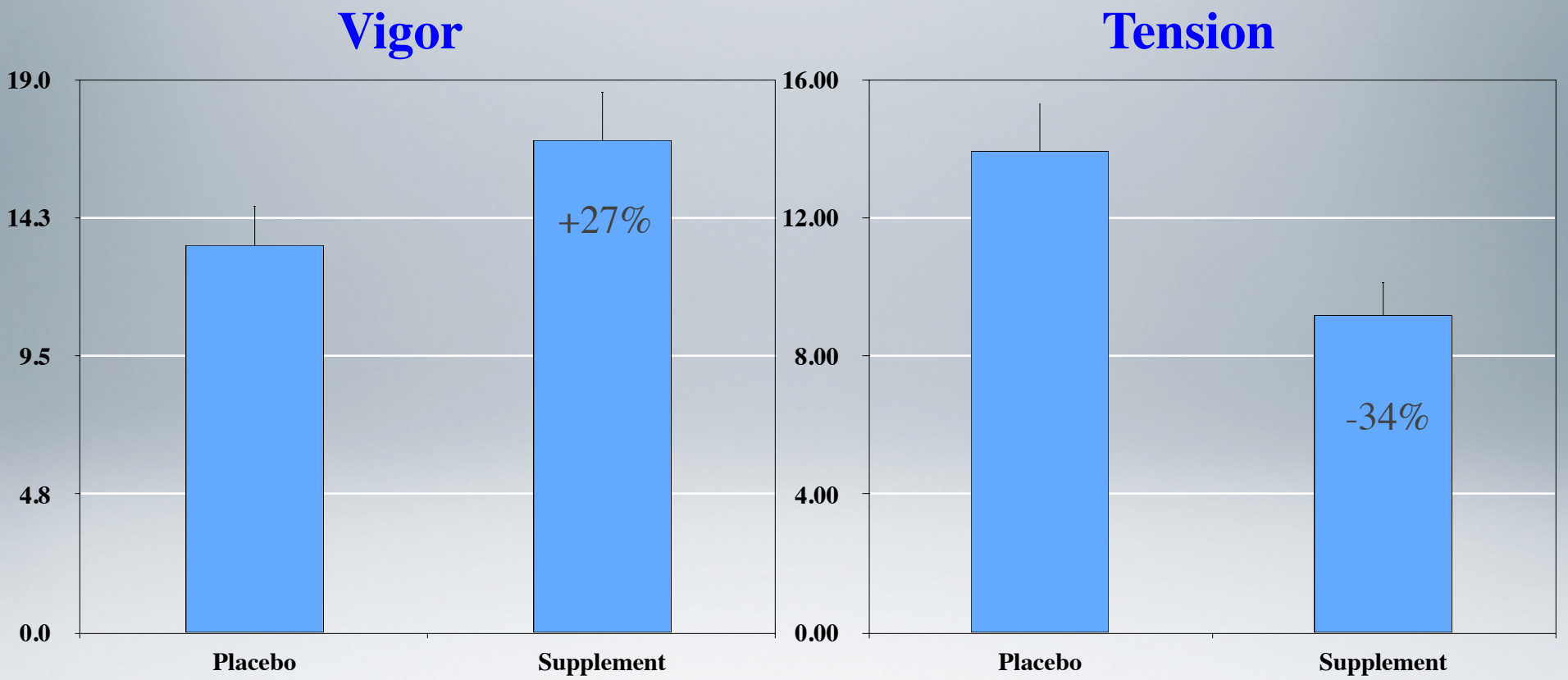
Both, $p \leq 0.05$ compared to Placebo

SUPPLEMENT WATCH
Supplement Decisions Made Easy

LifeVantage

RESULTS (week 4)

Profile of Mood States (POMS)



Both, $p \leq 0.05$ compared to Placebo

SUPPLEMENT WATCH
Supplement Decisions Made Easy

LifeVantage

Effect of *Eurycoma longifolia* Extract on Anabolic Balance During Endurance Exercise

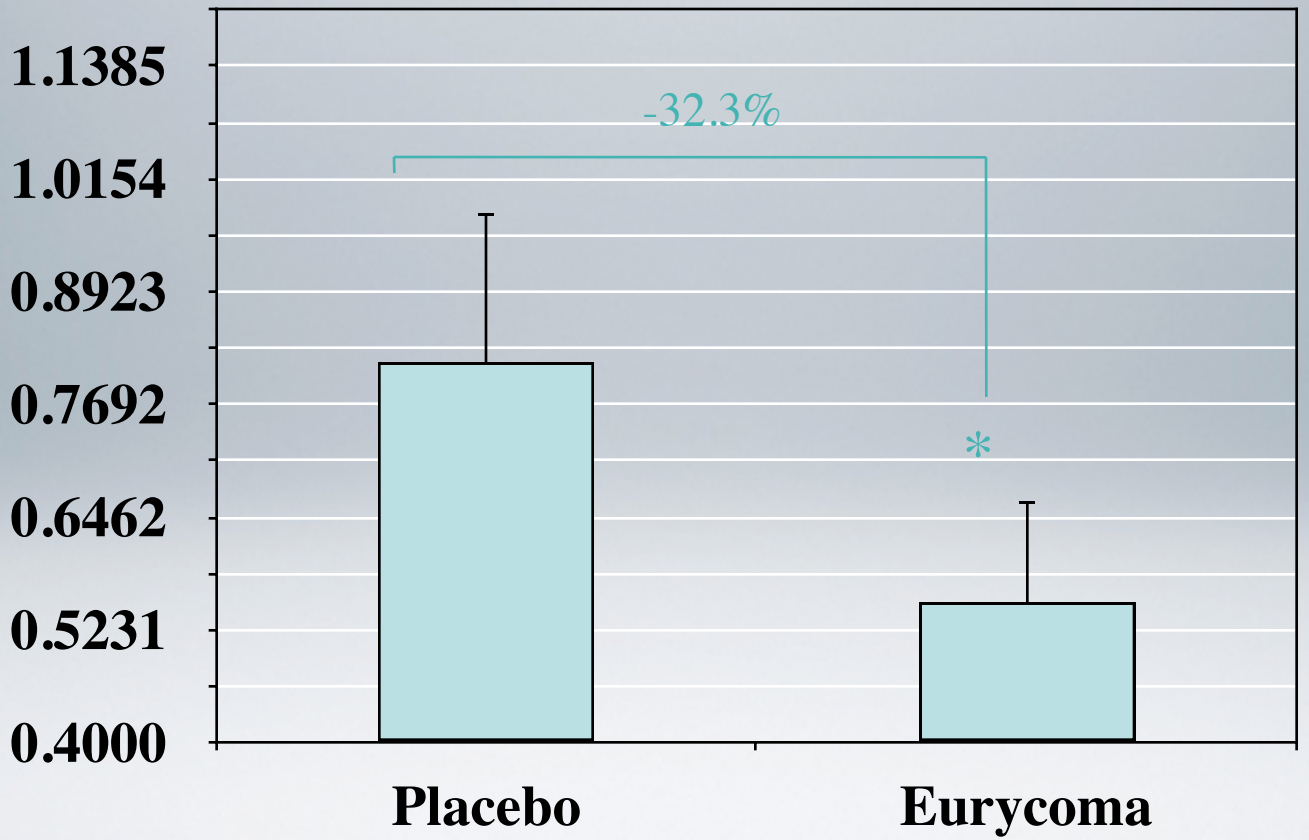
S. Talbott, J. Talbott, J. Negrete, M. Nichols, and J. Roza

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

& Source One Global, Chicago, IL

RESULTS

Salivary Cortisol (ug/dL)



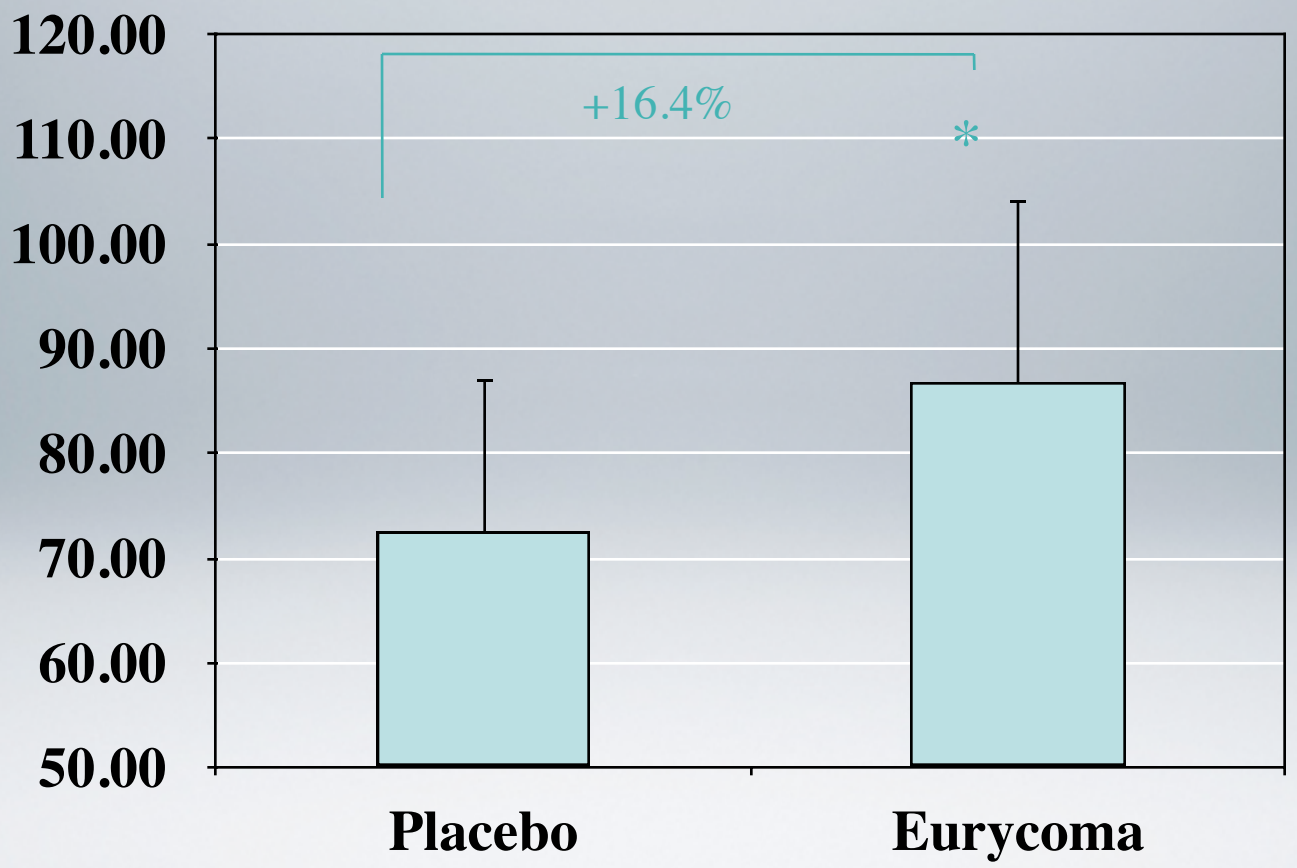
*p ≤ 0.05 compared to Placebo

SUPPLEMENT WATCH
Supplement Decisions Made Easy

LifeVantage

RESULTS

Salivary Testosterone (pg/dL)



*p ≤ 0.05 compared to Placebo

SUPPLEMENT WATCH
Supplement Decisions Made Easy

LifeVantage

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

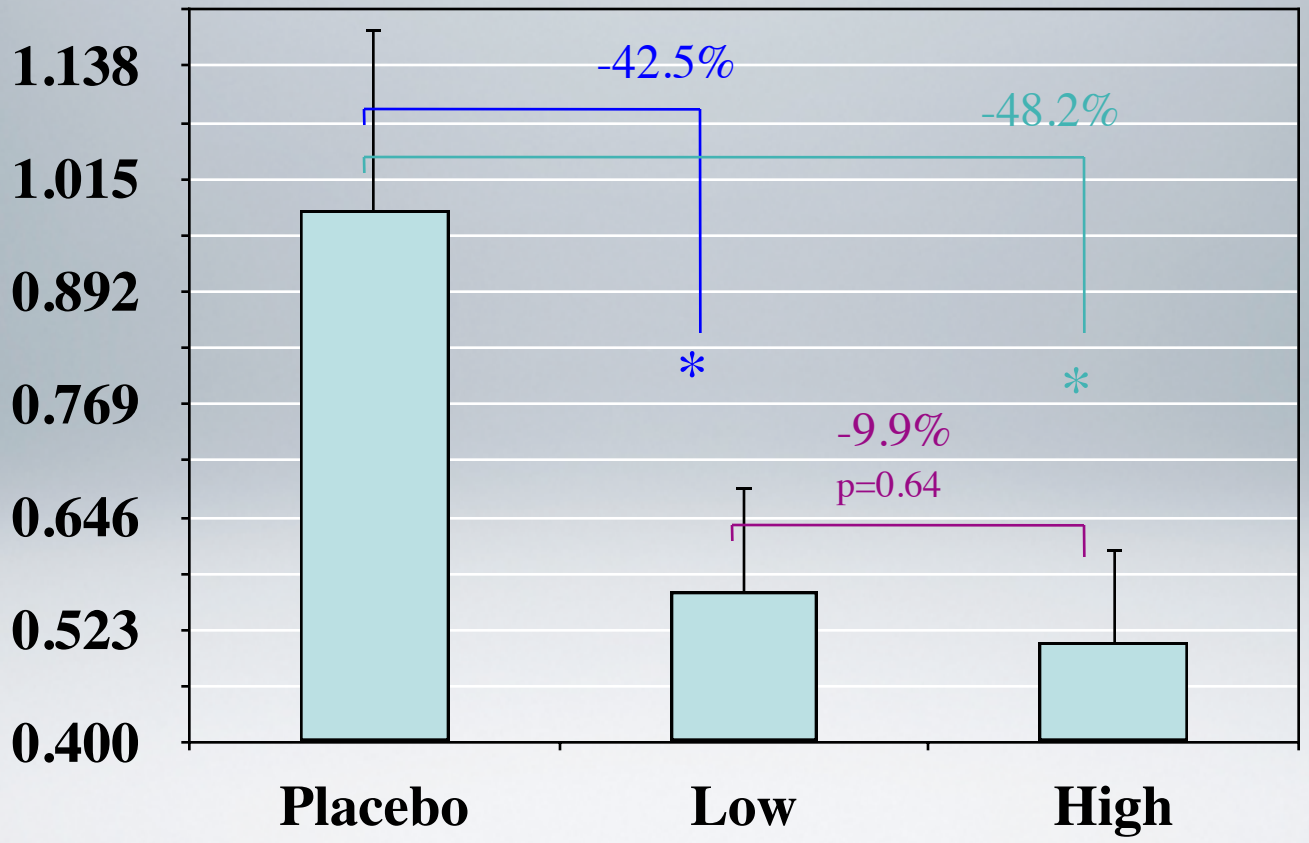
S. Talbott, J. Talbott, J. Negrete, and M. Nichols

SupplementWatch, Inc.

Salt Lake City (Draper), UT

RESULTS

Salivary Cortisol (ug/dL)



*p ≤ 0.05 compared to Placebo

SUPPLEMENT WATCH
Supplement Decisions Made Easy

LifeVantage

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

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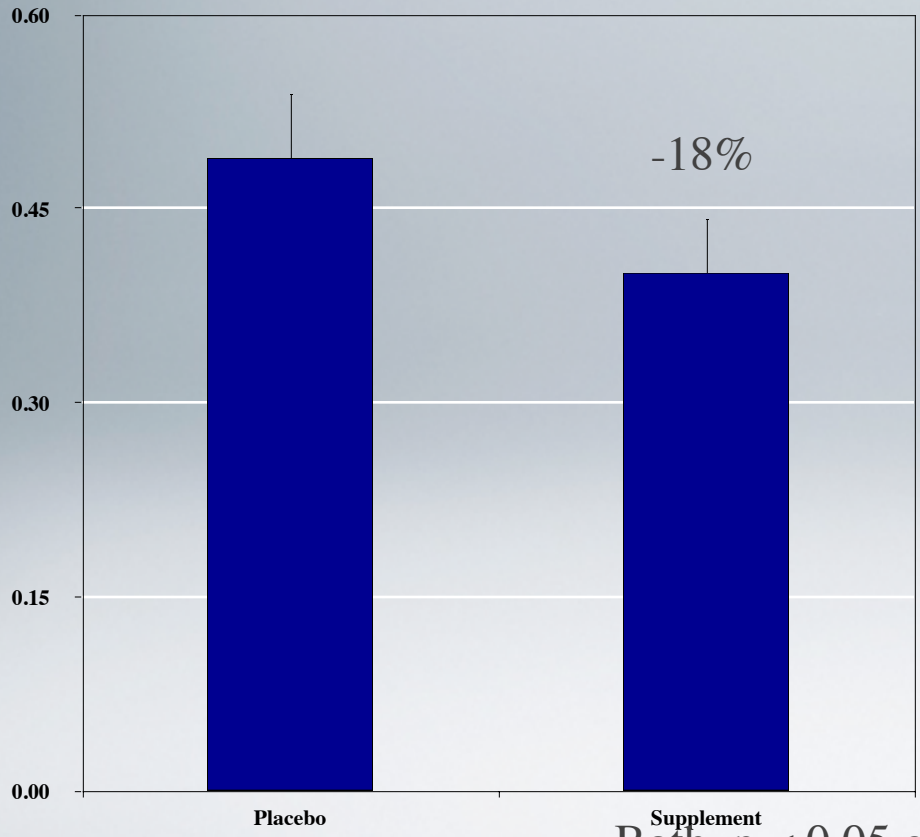
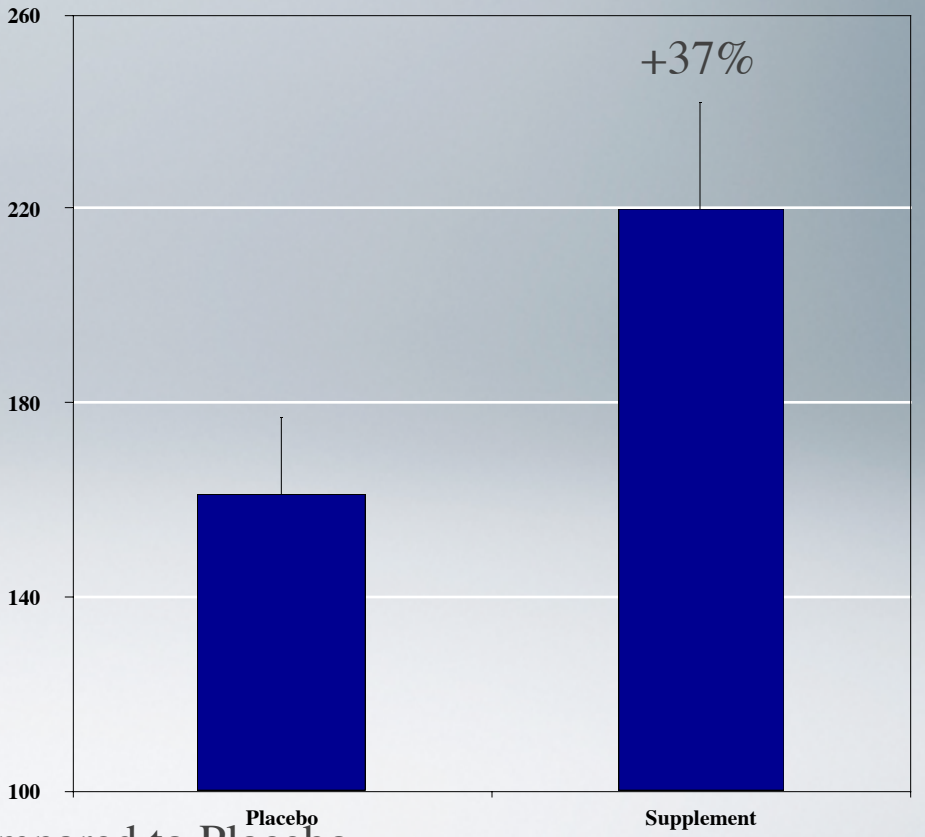
RESULTS (week 4)

Cortisol & Testosterone (% difference from Placebo)

Cortisol, ug/mL (Magnolia)



Testosterone, pg/mL (Eurycoma)



Both, $p \leq 0.05$ compared to Placebo

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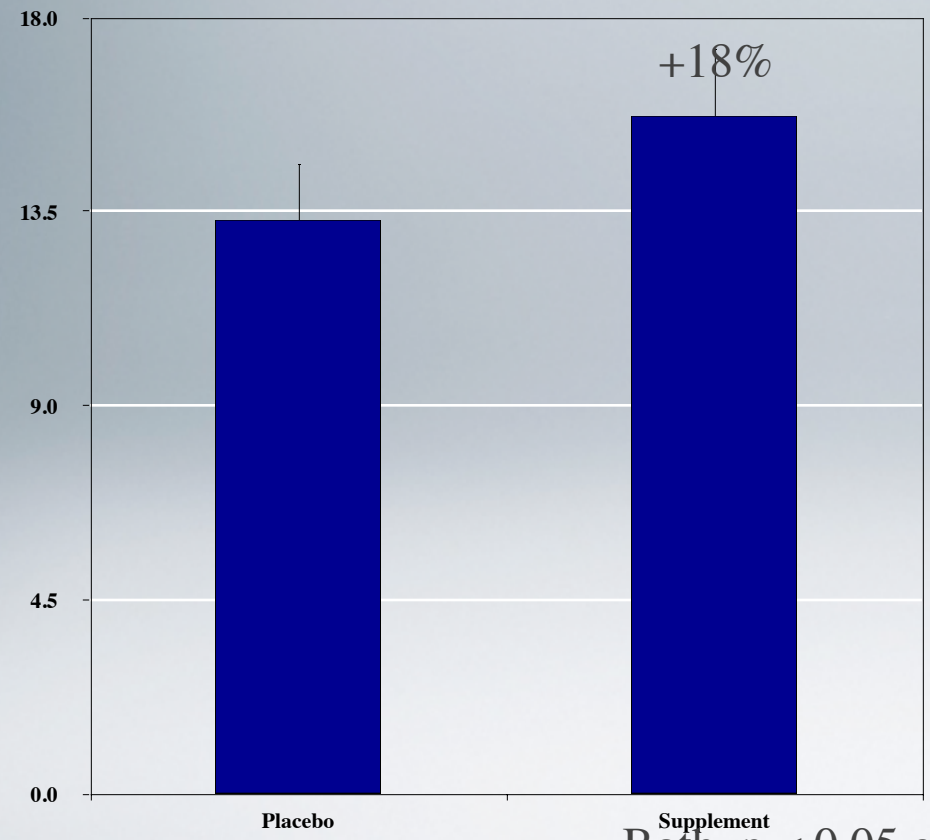
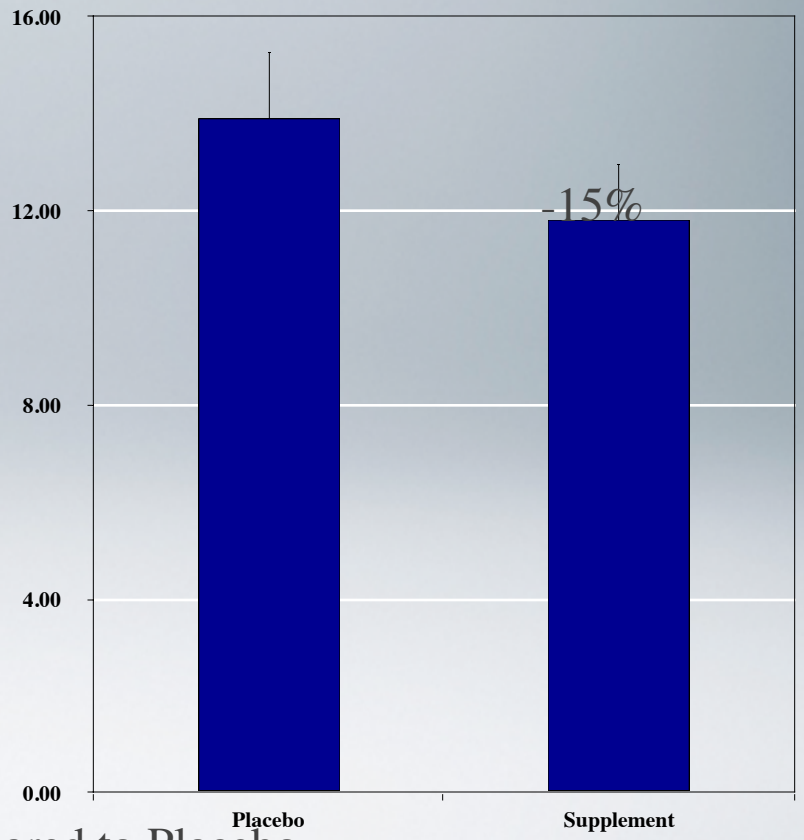
RESULTS (week 4)

Profile of Mood States (POMS)

Vigor (Magnolia)



Tension (Eurycoma)



Both, $p \leq 0.05$ compared to Placebo

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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)