

Workshop E5

**(Complementary and) Integrative Medicine:
Effective Herbal Therapies and other Approaches to
Primary Care Problems**

Primary Care Internal Medicine

21 October 2015 4:00-5:10 PM

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Harvard Medical School

Disclosure

I have no financial relationship
with a commercial entity
producing healthcare-related services

Donald B. Levy, M.D.

Integrative Medicine

A.K.A.

Holistic

Alternative

Complementary

Complementary and Alternative (CAM)

Complementary and Integrative (NCCIH)*

**National Center for Complementary and Integrative Health*

What is Modern Integrative Medicine?

.....health care with an attitude of mind that seeks *preferentially* those therapies or **therapeutic lifestyle changes (TLC)** that enhance one's **innate ability to recover from illness and maintain good health.**

(An incremental change in the approach and scope of Primary Care Medicine)

Integrative Medicine

- No single healing paradigm or tradition
- Roots in Western, Asian, naturopathic, manual, functional, nutritional and behavioral medicine.
- **Always guided and informed by scientific evidence and research**

Today's *Prepared Agenda*:
An Introduction to Integrative Medicine with a focus on
the **Rational Use of Dietary Supplements**

1. A Rational Approach

- Long Latency vs. Short Latency deficiency syndromes
- Determining an Optimal dose —i.e. Vitamin D
- **Case #1--Daily Multivitamins –helpful or harmful?**
- Finding high quality supplements
- The herbal “Entourage Effect”

2. Useful Supplements for several common conditions

- **Case #2--Hyperlipidemia**
- **Case #3--Hypertension**
- **Case #4--URI's/ Influenza: “I always get sick”**
- **Case #5--URI's/ Influenza: “What can I take?”**
- **Case #6—“I am tired, burned-out...stressed and depressed”**

Dietary Supplements:

Prevalence of Use in the United States

2003-2006: > 50% of Adults
> 32% of Children

1988-1994: 40% of Adults

Gahche J. et, al. **Dietary supplement use among U.S. adults has increased since NHANES III (1988-1994)**. NCHS data brief, no.61. Hyattsville, MD: National Center for Health Statistics. 2011

Picciano et al. **Dietary supplement use among infants, children and adolescents in the United States, 1999-2002**; *Arch Pediatr Adolesc Med.* 2007;161(10): 978-985

Three Rational Uses of Dietary Supplements

1. *Prevent or treat* an acute (**Short Latency**) deficiency condition
2. *Prevent or treat* a chronic (**Long Latency**) deficiency condition
3. *Treat* an acute or chronic disease
(“Green Pharmacy”)

For another day:

4. **Provide For Optimal Health** (very complex)
5. **Avoid toxicity** or interference with current medical therapy

Preventing or treating an Acute Deficiency or **Short Latency Syndrome**

May **1941**—NAS Subcommittee established **RDA's** to prevent acute deficiency syndromes in the general population. i.e. Take daily to prevent:

- **Scurvy** Vitamin **C** — **75-90 mg**
- **Rickets** Vitamin **D**— **600 IU**
- **Pellagra** Vitamin **B3** (Niacin) — **16 mg**
- **Berberi** Vitamin **B1** (Thiamin) — **1.2 mg**

However: What is the **optimal life-long dose of these vitamins?**

Preventing or treating a Chronic Disease or **Long Latency** Syndrome

There is suggestive evidence that specific vitamins, minerals or other supplements may *prevent, delay* or *ameliorate* :

- Osteoporosis
- Osteoarthritis
- Coronary Heart Disease
- Depression
- Hypertension
- Multiple Sclerosis
- Alzheimer's Disease
- Prostate Cancer
- Complications of Pregnancy

Fairfield KM, Fletcher RH. **Vitamins for chronic disease prevention in adults: scientific review.** JAMA. 2002 19;287(23):3116-26. Review

Holick MF. **Vitamin D deficiency.** NEJM. 2007;357(3):266-81. Review

Can We Really Prevent or Treat a Chronic Disease with a Micronutrient ?

If so, how do we investigate

Long Latency Hypotheses

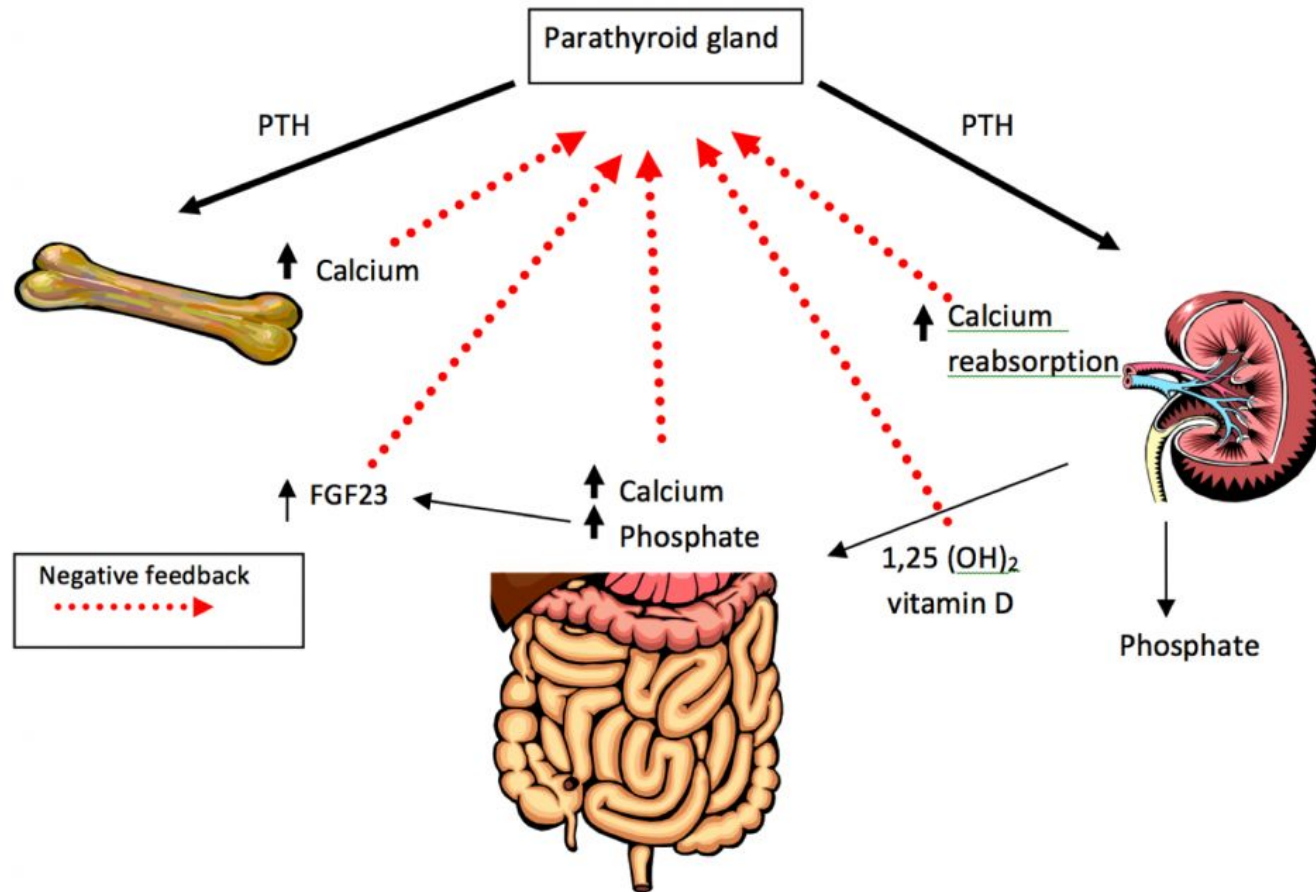
Without **VERY LARGE, 10-30 Year Studies?**

Hypothesis: **Osteoporosis is Partially Due to a Long latency Vitamin D Deficiency Syndrome**

Osteoporosis and Vitamin D Insufficiency:

- **Increased risk of falls**
- **Increased risk of vertebral and non-vertebral fractures**
- **Muscle weakness**

Look at physiologic feedback loops to determine what levels exist when there is optimal homoeostatic balance



Optimal Daily Dose of Vitamin D for Bone Health is likely When We See:

- ✓ **Maximal** Calcium Absorption and Transport
- ✓ **Lowest** Parathyroid Hormone (PTH) level
- ✓ **Greatest** Muscle Strength
- ✓ **Greatest** Bone Density

All of the Above are Achieved When:

Serum 25 (OH) D= Approx. 32 ng/mL* (80nmol/L)

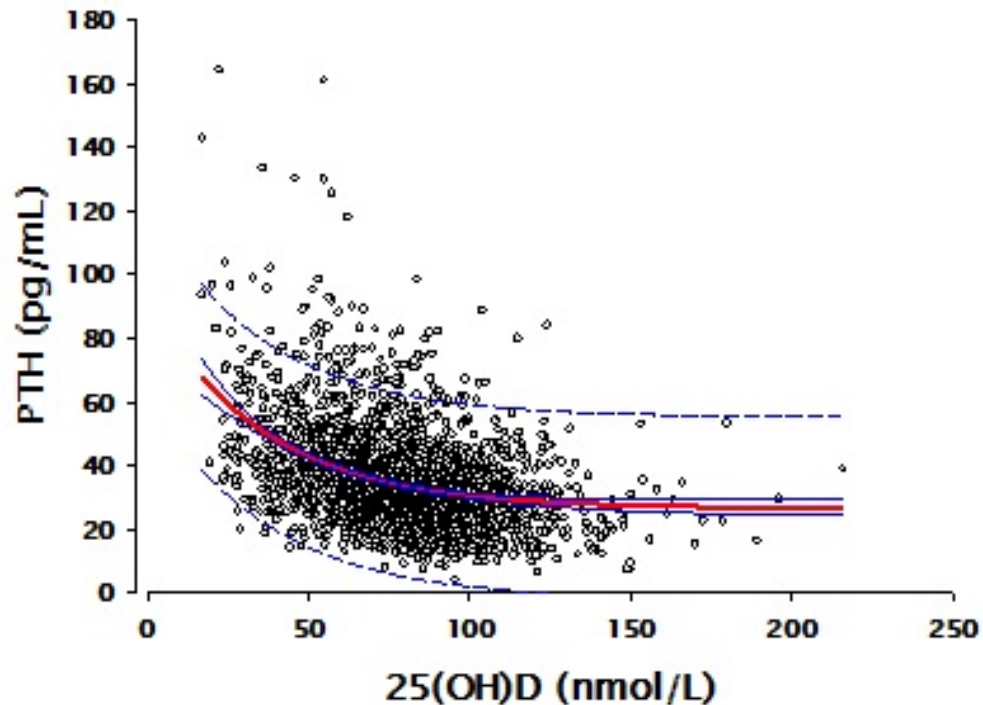
Ballpark optimal dose for bone homeostasis is whatever it takes to achieve that level.

Holick MF. **Vitamin D deficiency.** *NEJM.* 2007;357(3):266-81. Review.

*** Notes:**

- **I.O.M. Report** says data more consistent with level of **~20 ng/mL**
- **In sunny countries 25 (OH) D levels = 54-90 ng/mL**

PTH levels fall and level off as 25(OH) D levels rise



Rational Use of Vitamin D

Order a 25(OH) D Level

**Aim for level > 32 ng/mL
(80nmol/L)**

For many: every **1,000 IU of D3 daily**
raises 25(OH) D level *approx.* **10 ng/mL**

Case # 1: ***Daily*** Multivitamin/Multimineral ? (MVMM)

- “I Try to eat well...very busy...not always time to prepare a good meal...”
- “.... ***just for insurance?***”
- “but they say on the news there may be **danger:**

Fortmann SP et. al. **Vitamin and mineral supplements in the primary prevention of cardiovascular disease and cancer: an updated systematic evidence review for the U.S. preventive services task force.** *Ann Intern Med* 2013; 159(12):824-838

Multivitamins According to the Media

(Re: Fortmann SP et. al. *Ann Intern Med*, Dec 2013)

- Vitamins Lack Clear Health Benefits, **May Pose Risks** *Forbes*
- Studies suggest vitamins provide **no health benefits** *Fox Business News*
- How do Americans **waste \$28 billion a year?** On vitamins... *TIME*
- Docs Say **Stop Taking Multivitamins** *Associated Press*
- Do vitamins block disease? Some **disappointing news** *CBS Nightly News*
- Vitamins, mineral supplements deemed **waste of money** *CNN*
- Multivitamins **don't hold any health benefit**, experts say *Reuters*
- Multivitamins not tied to memory or heart benefits *The New York Times*
- Dr. Nancy: Forget multi-vitamins, just eat good food *USA Today*
- Medical journal: **'Case closed' against vitamin pills** *Wall Street Journal*
- Multivitamins found to have little benefit *WebMD*

Multivitamin-Multimineral (MVMM)

Some literature worth reading

- Fortmann SP et. al. **Vitamin and mineral supplements in the primary prevention of cardiovascular disease and cancer: an updated systematic evidence review for the U.S. preventive services task force.** Ann Intern Med 2013; 159(12):824-838

Macpherson H et.al. **Multivitamin-multimineral supplementation and mortality: a meta-analysis of randomized controlled trials.** Am J Clin Nutr 2013;97:437-44 .

Editorial comment: Chang SM. **Should meta-analyses trump observational studies?** Am J Clin Nutr 2013;97: 237-8.

Coates PM, Dwyer JT and Thurn AL. **Introduction to state-of-the-science conference: multivitamin/mineral supplements and chronic disease prevention.** Am J Clin Nutr 2007;85 (suppl):255S-6S.

Ames BN, McCann JC, Stampfer MJ and Willett WC. **Evidence-based decision making on micronutrients and chronic disease: long-term randomized controlled trials are not enough.** Am J Clin Nutr. 2007;86:522-5.

Horrobin D. **Why do we not make more medical use of nutrition knowledge? How an inadvertent alliance between reductionist scientists, holistic dietitians and drug-oriented regulators and government has blocked progress.** Brit J of Nutr. 2003;90:233-38

Fairfield KM, Fletcher RH. **Vitamins for chronic disease prevention in adults: scientific review.** JAMA. 2002; 287(23):3116-26. Review

Willett WC and Stampfer MJ. **What vitamins should I be taking, doctor?** NEJM. 2001;345(25): 1819-24

Nutrition experts are almost unanimous in suggesting:

The best path is to eat a fully balanced **diet** of high quality foods to obtain all the essential micronutrients

Many also admit:

In practice this is *nearly impossible to achieve*

Consensus of an Expert Panel Regarding Taking a MVMM

“Present evidence is insufficient to recommend *either for or against* ...to prevent chronic disease...”

.....the totality of scientific trials show that there is ***“no evidence of any safety issues or harm”*** from taking daily MVMMs.

Dissenting Experts :

“Certain **vulnerable populations
who likely do not get
all the essential micronutrients from diet should
definitely be advised to take a
M MMM. “**

Vulnerable Populations

- **Elderly**
- **Poor Urban-dwelling**
- **Pregnant or might become**
- **Vegans**
- **Drinking > 2 alcoholic beverages daily**
- **Hospitalized**
- **Mentally ill**

One “dissenting expert” worth reading:

Bruce Ames, Ph.D*



“Evidence is accumulating that a multivitamin/mineral supplement is good **insurance**, and would markedly improve health e.g., heart disease, cancer, immune function and cataracts...*particularly for those with inadequate diets* such as many of the **poor, young, obese and elderly**, who need improvement the most.”

Ames BN. **A role for supplements in optimizing health: the metabolic tune-up.** Arch Biochem Biophys. 2004;423(1):227-34. Review.

* *Prof. Emeritus of Biochemistry and Molecular Biology, University of California, Berkeley*

One Rational Daily Regimen for Adults

- **Multivitamin/Multimineral:** moderate doses—100%--200% of DRI
 - **Vitamin D3:** 1,000 units daily —or titrated to serum 25(OH) Vit D level >32 ng/mL
- (Omega-3 Fish Oil):** 1,000-2,000 mg. —especially if no fish in the diet
- (Micronutrients tailored to Age, Gender, FH):**
Ca+, B12, Probiotic, Lutein, Mg+ etc..

What About *Quality* ?

- **Quality, purity, potency and bioavailability vary tremendously!**
- **Some formulations may be more physiologic than others (Folate vs. methyltetrahydrofolate)**
- **Cost does not always reflect quality**

A *Start*: Look for these Product Seals



- Confirm the identity and quantity of ***some*** of the ingredients declared on the label
- Confirm product is free of ***selected*** contaminants and undeclared ingredients
- Demonstrate conformance to **industry** GMPs
- On-going **monitoring**

One Independent Distributor's *Quality Program*

www.emersonecologics.com



**Some of the Quality Supplement Brands
That are Available Through Retail Outlets***

Enzymatic Therapy

Gaia Herbs

Nature's Way

NOW Vitamins

Nordic Naturals (for fish oils, Omega-3 fatty acids)

Cost: Look on-line; i.e. www.vitacost.com

***Some of the highest quality brands of dietary supplements are available only through health care professionals.**

Rational Use of Dietary Supplements for some Common Conditions in Primary Care

Case # 2: Hyperlipidemia

Case #3: Hypertension

Case #4-5: Upper Respiratory Infections

Case #6: “Burned-out/ Stressed-out”

Case # 2a: **Hyperlipidemia—Statin intolerant**

but patient really needs this medication and willing to try

Consider:

Vitamin D—if deficient

Red Yeast Rice (see 1b)

Coenzyme Q10? —Current evidence suggests *no benefit for statin-induced myalgias*

2a. Hyperlipidemia—Statin intolerant: Vitamin D Supplementation

- Check 25(OH) D level
 - Supplement if level below 32 ng/mL (80 nMol)
- Michalska-Kasiczak M, et. al. **Analysis of vitamin D levels in patients with and without statin-associated myalgia - A systematic review and meta-analysis of 7 studies with 2420 patients.** Int J Cardiol. **2014**;178C:111-116
- Waqas A et. al. **Low serum 25(OH) vitamin D levels (<32 ng/mL) are associated with reversible myositis-myalgia in statin-treated patients.** Translational Res 2009;153:11-16.
 - Lee, P et. al. **Vitamin D insufficiency--a novel mechanism of statin-induced myalgias?** Clin Endocrinology 2009.71;151-156

2a. Hyperlipidemia— Statin intolerant Co-Enzyme Q10 ?

Safe, nutritionally reasonable, but latest trials speak against significant benefit for statin-induced myalgias

- Taylor BA et. al. **A randomized trial of coenzyme Q10 in patients with confirmed statin myopathy.** *Atherosclerosis*. **2015** Feb;238(2):329-35. (Epub ahead of print)
- Banach M et. al. **Effects of coenzyme Q10 on statin-induced myopathy: a meta-analysis of randomized controlled trials.** *Mayo Clin Proc*. **2015** Jan;90(1): 24-34
- Caso G et. Al. **Effect of coenzyme q10 on myopathic symptoms in patients treated with statins.** *Am J Cardiol* **2007**;99(10): 1409-12
- Marcoff L, Thompson PD. **The role of coenzyme Q10 in statin-associated myopathy: a systematic review.** *J Am Coll Cardiol*. **2007** ;49(23): 2231-7

Case # 2b: **Hyperlipidemia**— “No statin please!”

The individual who *cannot* or *will not* take a statin

Therapeutic Lifestyle Changes--especially Diet-Classic Mediterranean (Lyon Diet Heart Study) + **Soluble Fiber** (Psyllium, oat, flaxseed) + nuts

Plant Stanols and sterols

Red Yeast Rice

Nuts

Niacin --still benefit if *not already on a statin* (*Coronary Drug Project—1980's*)

Theaflavin-enriched Green Tea Extract (1 RCT)

Policosanol

Guggulipid (Both unlikely to be helpful based on good studies)

Hyperlipidemia: Plant Stanols and Sterols

(Present in Western diet in small amounts--250-500 mg/d)

- **Can lower LDL cholesterol by 10-14% in doses of 2,000-3,000 mg /daily**
- **Well tolerated; does not affect serum levels of fat-soluble vitamins**

Amir Shaghghi M. **Cholesterol-lowering efficacy of plant sterols/stanols provided in capsule and tablet formats: results of a systematic review and meta-analysis.** J Acad Nutr Diet.2013;113(11): 1494-503

Talati R et. al. **The comparative efficacy of plant sterols and stanols on serum lipids: a systematic review and meta-analysis.** J Am Diet Assoc.2010;110(5):719-26

Katan MB, Grundy SM, et. al. **Efficacy and safety of plant stanols and sterols in the management of blood cholesterol levels.** Mayo Clin Proc. 2003;78(8):965-78. Review.

Hyperlipidemia: Plant Stanols and Sterols

Note: 450 mg. per cap. (*Need 5 daily not 4*)



Hyperlipidemia: Red Yeast Rice

Dietary staple in some countries and used for 13 centuries in China--contains plant sterols, isoflavones and naturally occurring statins (monacolins)

- Trials using a **dose of 2.4 --3.6 grams daily** lasting at least **6 months** have shown it to be well tolerated **even in patients who had previously been statin- intolerant**
- **20-25% reductions in LDL cholesterol**
- Study of almost 5,000 patients in China with previous MI; 4.5 years; **Decreased Cardiac events and CVD mortality**
- **Must be high quality product to avoid contaminant (citrinin)**

Red Yeast Rice: Literature

- Moriarty PM. **Effects of Xuezhikang in patients with dyslipidemia: a multicenter, randomized, placebo-controlled study.** J Clin Lipidol. 2014;8(6):568-75
- Li Y. **A meta-analysis of red yeast rice: an effective and relatively safe alternative approach for dyslipidemia.** PLoS One. 2014;9(6):e98611
- Becker DJ et. al. **Phytosterols, red yeast rice, and lifestyle changes instead of statins: a randomized, double-blinded, placebo-controlled trial.** Am Heart J. 2013;166(1):187-96
- Becker DJ et. al. **Red yeast rice for dyslipidemia in statin-intolerant patients.** Ann Intern Med. 2009;150:830-839.
- Verhoeven V et. al. **Red yeast rice lowers cholesterol in physicians - a double blind, placebo controlled randomized trial.** BMC Complement Altern Med. 2013;13(1):178
- Lu Z et al. **Effect of Xuezhikang, an extract from red yeast rice, on coronary events in a Chinese population with previous myocardial infarction.** Am J Cardiol. 2008;101(12):1689-93

Hyperlipidemia: Nuts!

- **Substituting a handful of almonds, walnuts, hazelnuts, pistachios and other nuts** for isocaloric foods lowers cholesterol in a dose-related manner
- **May Reduce the risk of CHD** to a degree beyond that expected from cholesterol-lowering alone.
- May exert beneficial effects by improving **endothelial function, lowering oxidative stress, lowering the risk type 2 diabetes** or by ?

- Nishi SK et.al. **Nut Consumption, serum fatty acid profile and estimated coronary heart disease risk in type 2 diabetes.** Nutr Metab Cardiovasc Dis. 2014;24(8):845-52
- Orem A et. al. **Hazelnut-enriched diet improves cardiovascular risk biomarkers beyond a lipid-lowering effect in hypercholesterolemic subjects.** J Clin Lipidol. 2013;7(2):123-31
- Sabate J, et. al. **Nut consumption and blood lipid levels: a pooled analysis of 25 intervention trials.** Arch Intern Med. 2010;170(9):821-7
- Gebauer SK et. al. **Effects of pistachios on cardiovascular disease risk factors and potential mechanisms of action: a dose-dependent study.** Am J Clin Nutr. 2008;88(3):651-9
- Zambon D **Substituting walnuts for monounsaturated fat improves the serum lipid profile of hypercholesterolemic men and women. A randomized crossover trial.** Ann Intern Med.2000;132(7):538-

Case # 3. **Hypertension:**

Non-Pharmacologic Management always begins with:

Therapeutic Lifestyle Changes

- **Exercise/physical activity**
- **Diet: “DASH”**
- **ETOH**

DASH Diet: Literature

- Salehi-Abargouei A et al. **Effects of Dietary Approaches to Stop Hypertension (DASH)-style diet on fatal or nonfatal cardiovascular diseases--incidence: a systematic review and meta-analysis on observational prospective studies.** Nutrition. 2013;29(4):611-8. Review.
- Elmer PJ et. al. PREMIER Collaborative Research Group. **Effects of comprehensive lifestyle modification on diet, weight, physical fitness, and blood pressure control: 18-month results of a randomized trial.** Ann Intern Med. 2006;144(7):485-95
- Sacks FM,et al. **A dietary approach to prevent hypertension: a review of the Dietary Approaches to Stop Hypertension (DASH) Study.** Clin Cardiol. 1999;22 (7 Suppl):III6-10

Sample (partial) handout:

Good Food Sources of Potassium

Cantaloupe

Dates

Honeydew melon

Dried Apricots

Raisins

Banana

Oranges

Avocado

Acorn/winter squash

Artichoke

Baked beans

Broccoli

Chick peas

Potato

Tomato paste/sauce

Hypertension

Beyond Medications and Diet

Mind-Body Therapies as Adjuvants:

- ◆ Mindfulness Meditation, Biofeedback, Tai Chi; Yoga; Resperate device
- ◆ Acupuncture trial

Rational Supplements:

- Magnesium citrate
- Tomato/Tomato extract
- (Coenzyme Q10)
- (Quercetin)

Mind-Body Techniques as *Adjuvants*

*Varying styles/approaches = Heterogeneity of Literature;
Some great responders with multiple benefits*

- **Mindfulness Meditation; Yoga**
- **Biofeedback; *RESPeRATE*™**
- **Tai Chi / Qi Gong**

Bisognano et al. **Beyond Medications and Diet: Alternative Approaches to Lowering Blood.** Scientific Statement From the American Heart Association Hypertension. **2013**;1360-83

Blom et al. **Hypertension analysis of stress reduction using mindfulness meditation and yoga: results from the harmony randomized controlled trial.** Am J Hypertens. **2014**;27(1):122-9.

de fatima Rosas Marchiori. **Decrease in blood pressure and improved psychological aspects through meditation training in hypertensive older adults: a randomized control study.** Geriatr Gerontol Int. **2014**

Wang J et al. **Tai chi for essential hypertension.** Evid Based Complement Alternat Med. **2013**:215254

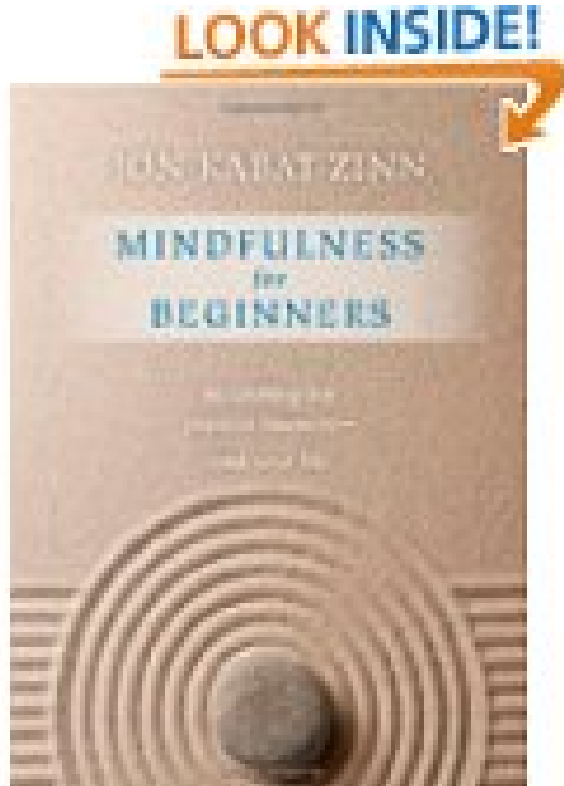
Cramer H, et al. **A systematic review and meta-analysis of yoga for hypertension.** Am J Hypertens. **2014**; 27(9):1146-51.

Cernes R. **RESPeRATE: the role of paced breathing in hypertension treatment.** J Am Soc Hypertens. **2014**

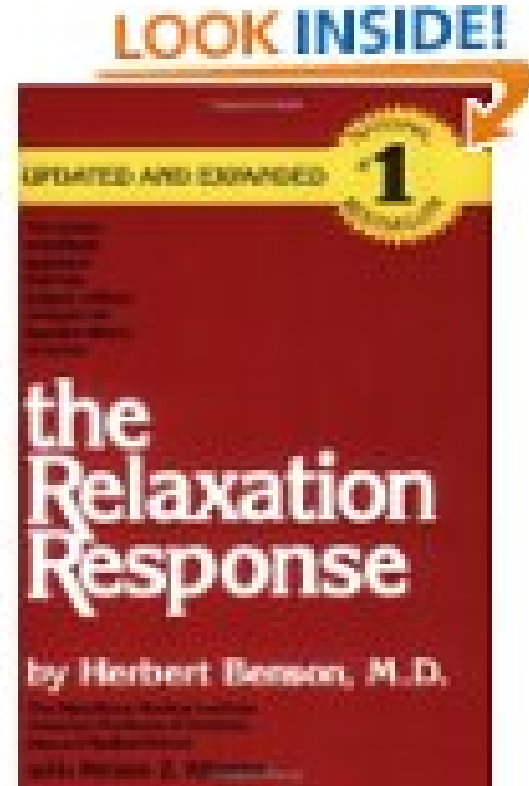
Nakao M, et al. **Blood pressure-lowering effects of biofeedback treatment in hypertension: a meta-analysis of randomized controlled trials.** Hypertens Res. 2003;26(1):37-46

Two Popular Types of Mindfulness Training

Jon Kabat-Zinn



Herbert Benson



Common Aspects of Mindful Awareness Practice (i.e. Meditation)

- **Intention**
- **Focusing the attention via** some form of **repetition** or return to focus
- **Nonjudgmental attitude** toward everything experienced

Mindfulness Practice (Meditation) Alters Brain *Function*

May strengthen the ability to
choose where to put attention
and then to keep it there

(“Protecting your mind from hijacking”)

Regular Meditation also Alters Brain *Structure*

(A Likely result of
Neuroplasticity)

Mindfulness, Tai Chi, Yoga Literature

- Bisognano et al. **Beyond Medications and Diet: Alternative Approaches to Lowering Blood. Scientific Statement From the American Heart Association** Hypertension. **2013**;1360-83
- Blom et al. **Hypertension analysis of stress reduction using mindfulness meditation and yoga: results from the harmony randomized controlled trial.** Am J Hypertens. **2014**;27(1):122-9.
- de fatima Rosas Marchiori. **Decrease in blood pressure and improved psychological aspects through meditation training in hypertensive older adults: a randomized control study.** Geriatr Gerontol Int. **2014**
- Cramer H, et. al. **A systematic review and meta-analysis of yoga for hypertension.** Am J Hypertens. **2014**; 27(9):1146-51.
- Cernes R. **RESPeRATE: the role of paced breathing in hypertension treatment.** J Am Soc Hypertens. **2014**
- Nakao M, et. al. **Blood pressure-lowering effects of biofeedback treatment in hypertension: a meta-analysis of randomized controlled trials.** Hypertens Res. 2003;26(1):37-46
- Wayne, Peter. **Harvard Medical School Guide to Tai Chi.** **2013**; Shambala Publications
- Wang J et. al. **Tai chi for essential hypertension.** Evid Based Complement Alternat Med. **2013**:215254
- Wang F. et. al. **The effects of tai chi on depression, anxiety, and psychological well-being: a systematic review and meta-analysis.**Int J Behav Med. **2013**
- Esch T. et. al. **Mind/body techniques for physiological and psychological stress reduction: stress management via Tai Chi training - a pilot study.** Med Sci Monit. 2007;13(11):CR488-497

Mindfulness and Breathing

RESPeRATE™ Device





RESPeRATE in Use

Guided paced breathing: (1) monitoring breathing movements, (2) composing breathing-guiding tones, and (3) synchronizing breathing

From: Cernes. J Am Soc Hypertens 2014;S1933-1711(14) 00834-1

Magnesium

- Magnesium Citrate or glycinate well absorbed
- Often a good *adjunct* to ongoing care
- Dose: **400-600 mg**; May take 6 weeks to show effect

Afsar B. **The relationship between magnesium and ambulatory blood pressure, augmentation index, pulse wave velocity, total peripheral resistance, and cardiac output in essential hypertension patients.** J Am Soc Hypertens. 2014;8(1):28-35

Kolte D. **Role of magnesium in cardiovascular diseases.** Cardiol Rev. 2014;22(4):182-92

Rodriquez-M M.. Arch Med Res. 2014;45(5):388-93**Oral magnesium supplementation improves the metabolic profile of metabolically obese, normal-weight individuals: a randomized double-blind placebo-controlled trial**

Rosanoff A. **Oral magnesium supplements decrease high blood pressure (SBP>155 mmHg) in hypertensive subjects on anti-hypertensive medications: a targeted meta-analysis.** Magnes Res. 2013;26(3):93-9

Bo S **Role of dietary magnesium in cardiovascular disease prevention, insulin sensitivity and diabetes.** Curr Opin Lipidol. 2008;19(1):50-6.

Magnesium: “Side effects”

Depends on **dose** and **formulation**

Magnesium Citrate
2 caps = 500 mg



Magnesium Citrate *Laxative*
1 bottle = 17,450 mg



Tomato Extract

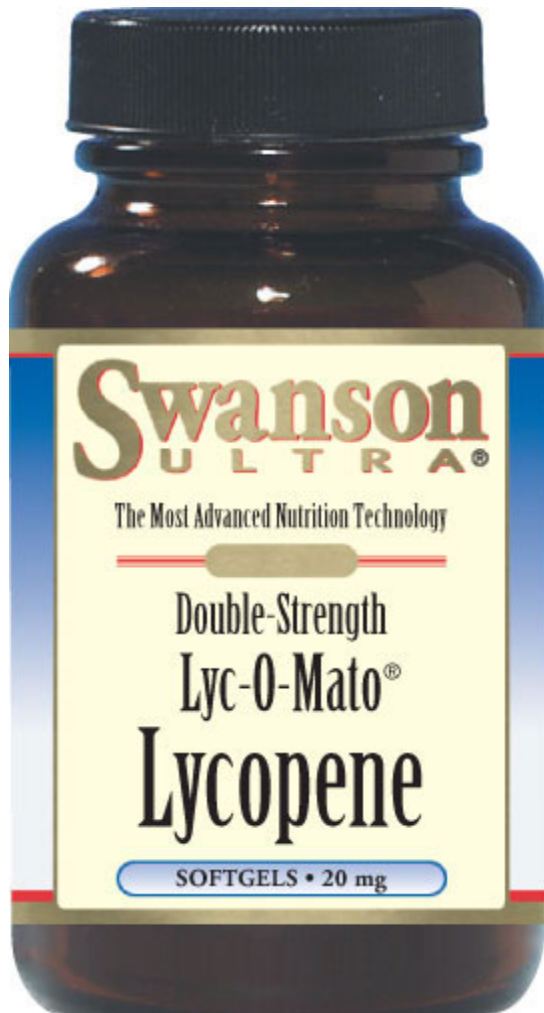
- **Lycopene** content : 15-20 mg daily
- Is it the **Lycopene** or the ***whole extract?***

Paran E. et. al. **The effects of natural antioxidants from tomato extract in treated but uncontrolled hypertensive patients.** Cardiovasc Drugs Ther. 2009;23(2):145-51

Engelhard YN et al. **Natural antioxidants from tomato extract reduce blood pressure in patients with grade-1 hypertension: a double-blind, placebo-controlled pilot study.** Am Heart J. 2006;151(1):100

Tomato Extract: *Lyc-O-Mato*TM

Is it the Lycopene or the whole extract? (“Entourage effect”)



Supplement Facts

Serving Size 1 Softgel

	Amount Per Serving	% Daily Value
Lyc-O-Mato [®] Tomato Extract (100%) Providing	334 mg	*
Lycopene (6%)	20 mg	*
Natural Tocopherols (1.5%)	5 mg	*
Phytoene and Phytofluene (1%)	3.33 mg	*

*Daily Value not established.

Other ingredients: Soybean oil, gelatin, glycerin, purified water, beeswax, carob.

Suggested use: As a dietary supplement, take one softgel per day with water and food.



Lyc-O-Mato[®] is a registered trademark of LycoRed Natural Products Industries Ltd.



Pharmaceutical vs. Herbal remedies

Are herbal remedies simply “messy” drugs?

Pharmaceuticals

- Usually have 1 or 2 chemical compounds: isolated, identified, measured
- Impurities or less active ingredients removed

Herbal extracts

- Contain numerous chemical compounds
- Not all identified, isolated, measured

For example: A current scientific /social dilemma:
Medical Marijuana (*Cannabis sativa*)

Plant composition:

1. THC— Tetrahydrocannabinol

2. CBD— Cannabidiol

3. CBG—Cannabigerol

4. CBN—Cannabinol

5. CBC—Cannabichromene

6. THCV—Tetrahydrocannabivarin

+ 66 other Cannabinoids

+ **Terpenoids**, Amino acids, Proteins, Sugars, Enzymes, Fatty acids, Esters, Flavonoids.....

The “Entourage Effect”

The synergistic interaction of numerous chemical constituents

1. THC considered the “*Psychoactive ingredient*”
but...

2. CBD (cannabidiol) modifies the effects of THC

- Blocks anxiety caused by THC
- High CBD= less psychotic experiences
- Attenuates memory impairment
- (Potent anti-inflammatory)

“Attempts to isolate the active principles from plant extracts may be ultimately self-defeating”

- “The presence of several psychoactive compounds in one plant may have a ‘synergistic’ effect...”
- The **‘silver bullet’ concept** adopted by orthodox Western medicine for the drug discovery over the past 100 years, is now increasingly viewed as inadequate in many clinical situations...”

From: Sarris J et. al. **Herbal medicine for depression, anxiety and insomnia: a review of psychopharmacology and clinical evidence.**

Eur Neuropsychopharmacol. 2011;21:841-860

Update: Hypertension and Vitamin D

LATEST LITERATURE: No benefit in supplementing Vitamin D deficiency in Hypertension

- Scragg R, Long-term high-dose vitamin D3 supplementation and blood pressure in healthy adults: a randomized controlled trial. Hypertension. **2014** ;64(4):725-30.
- Arora P, et. al. Vitamin D Therapy in Individuals With Prehypertension or Hypertension: The DAYLIGHT Trial. Circulation. **2015** ;131(3):254-62

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- Andrukhova O et al. Vitamin d as a regulator of endothelial nitric oxide synthase and arterial stiffness in mice. Mol Endocrinol. 2014;28(1): 53-64
 - Banzato C et al. Hypovitaminosis d and nocturnal hypertension in obese children: an interesting link. J Hum Hypertens. 2013;1-7
 - Min B. Effects of vitamin d on blood pressure and endothelial function. Korean J Physiol Pharmacol. 2013;17(5):285-92
 - Pilz S et al. Vitamin D status and arterial hypertension: a systematic review . Nat Rev Cardiol. 2009;6 (10): 621-30

Still reasonable to Check a 25(OH) D level

- Supplement only if low (<32 ng/mL)-- for other health benefits**

Acupuncture



Some people respond especially as an **adjunctive therapy**: worth a defined therapeutic trial

Longhurst J. **Acupuncture's Cardiovascular Actions: A Mechanistic Perspective**. Med Acupunct. **2013** ;25(2):101-113. Review.

Li DZ... . **Acupuncture for essential hypertension: a meta-analysis of randomized sham-controlled clinical trials**. Evid Based Complement Alternat Med. 2014; **2014**:279478.

Longhurst JC, **Acupuncture regulation of blood pressure: two decades of research**. Int Rev Neurobiol. **2013**;111:257-71

Yin C et. al. **Acupuncture, a promising adjunctive therapy for essential hypertension: a double-blind, randomized, controlled trial**. Neurol Res. 2007;29 Suppl 1:S98-103

Wang J. **Acupuncture for essential hypertension**. Int J Cardiol. 2013;169(5):317-26

Lee H et. al. **Acupuncture for lowering blood pressure: systematic review and meta-analysis**. Am J Hypertens. 2009 22(1):122-8

“More rigorous trials are warranted.....”

Hypertension: Supplements to watch for additional literature

- **Coenzyme Q10 (C0Q10):** A naturally occurring, fat soluble enzyme found in every cell in the body—an antioxidant involved in multiple cellular processes

Rosenfeldt F, et al. **Systematic review of effect of coenzyme Q10 in physical exercise, hypertension and heart failure.** Biofactors. 2003;18(1-4):91-100. Review.

- **Quercetin:** An antioxidant flavanol found in apples berries and onions

Edwards RL, et al. **Quercetin reduces blood pressure in hypertensive subjects.** J Nutr. 2007 137(11):2405-11

- **Pycnogenol (French maritime pine bark)** Herb with antioxidant, anti-inflammatory and vasodilator properties; May **augment the effect of a medication:** 100 mg. daily for 12 weeks helped reduce the dose of nifedipine

Liu X, et al. **Pycnogenol, French maritime pine bark extract, improves endothelial function of hypertensive patients.** Life Sci. 2004 ;74(7):855-62

- **Potassium supplementation...** Judicious, monitored (?)

Rational Use of **Therapeutic Lifestyle Changes**

Is it too late....
by the time a **middle-aged**
patient with **hypertension**
arrives in the office ?

Turning Back the Clock: Adopting a Healthy Lifestyle in Middle Age

- 1. Fruits/Vegetables— 5 servings/day**
- 2. Exercise— 2.5 hours/week (at least walking)**
- 3. Weight Control –(BMI= 18.5—30.0)**
- 4. No Smoking**

Next 4 years:

Decreased mortality (2.5% vs. 4.2%)

Decreased cardiovascular Disease (11.7% vs. 16.5%)

Dana et. al. *Am J Med.* 2007; 120: 598-603

3. Upper Respiratory Infections

**Offering a Patient Something Rationale
For Prevention or Treatment**

Rather Than

**the often unnecessary, inappropriate,
but requested antibiotic**

Case #4: **“I always get sick”**

Reasonable Evidence for **Preventing** a URI

- ✓ **Exercise-- Moderate daily**
- ✓ **Handwashing—also outside the hospital***
- **Diet +/- multivitamin**
- **Green Tea Extract formulations**
- **Probiotics— growing literature**
- **Quercetin**
- **Vitamin D** (if deficient)
- **Vitamin C** (special cases; doses)
- **Zinc** (oral, dissolving , may be effective)

Highest Hotel room microflora: TV Remote, Telephone, Alarm clock, Bathroom faucet, Thermostat, Ice bucket, Door handles, Bible

URI—**Prevention**: Quercetin

Dietary flavonol found in **apples, onions, berries, black tea, leafy green vegetables and red grapes**

Antioxidant, anti-inflammatory, antihistamine and antiviral properties.

Nieman DC et al. **Quercetin reduces illness but not immune perturbations after intensive exercise.** Med Sci Sports Exerc. 2007;39(9):1561-9

- *Physically stressed cyclists were given **500 mg. bid**, they had significantly fewer upper respiratory tract infections despite no changes in several measures of immune function*

Heinz SA. **Quercetin supplementation and upper respiratory infection: A randomized community clinical trial.** Oharmacol Res. 2010; 62(3):237-42

- *A reduction in URI related sick days and severity noted in middle-aged and older subjects **taking 1000 mg/day** who rated themselves as physically fit*

(Much of the literature = animal models or tissue culture)

URI—Prevention: Green Tea Extract

Randomized, controlled trial of a proprietary formulation

Two capsules daily –equivalent to drinking about 10 cups daily—for 3 months.

Significant decrease in the incidence of cold and flu illnesses and for those who became ill, a significant decrease in the number of days that subjects had symptoms. *Interestingly, there was not a prolonged increase in certain T cell subsets or interferon levels, but there was a vigorously enhanced response of T cell function when there was an antigenic challenge.*

Rowe CA, Nantz MP, Bukowski JF, Percival SS. **Specific formulation of Camellia sinensis prevents cold and flu symptoms and enhances gamma, delta T cell function: a randomized, double-blind, placebo-controlled study.** J Am Coll Nutr. 2007; 26(5):445-52

(There is an additional literature base on green tea and infection/inflammation, i.e:)

- Matsumoto K. **Effects of green tea catechins and theanine on preventing influenza Infection among healthcare workers.** BMC Complement Altern Med. 2011; Feb21
- Park M. **Green tea consumption is inversely associated with the incidence of influenza Infection among school children in a tea plantation area of Japan.** J Nutr.2011; 141(10)



Case # 5: “I am coming down with a cold; I need an antibiotic or something...now!”

- Herbal preparations: many claims
- Some have actually been tested and are especially effective when just becoming ill with a viral-type URI....rather than the often unnecessary, inappropriate, but requested antibiotic

Black Elderberry Extract (*Sambucus nigra*)

- Clinically: reduces symptoms when administered to patients with **influenza**
- **Anthocyanins** readily detected in bloodstream following ingestion
- May **inhibit neuraminidase** to roughly same degree as prescription meds
- Studied by mass spectrometry and molecular docking in **cell culture *and in clinical trials***

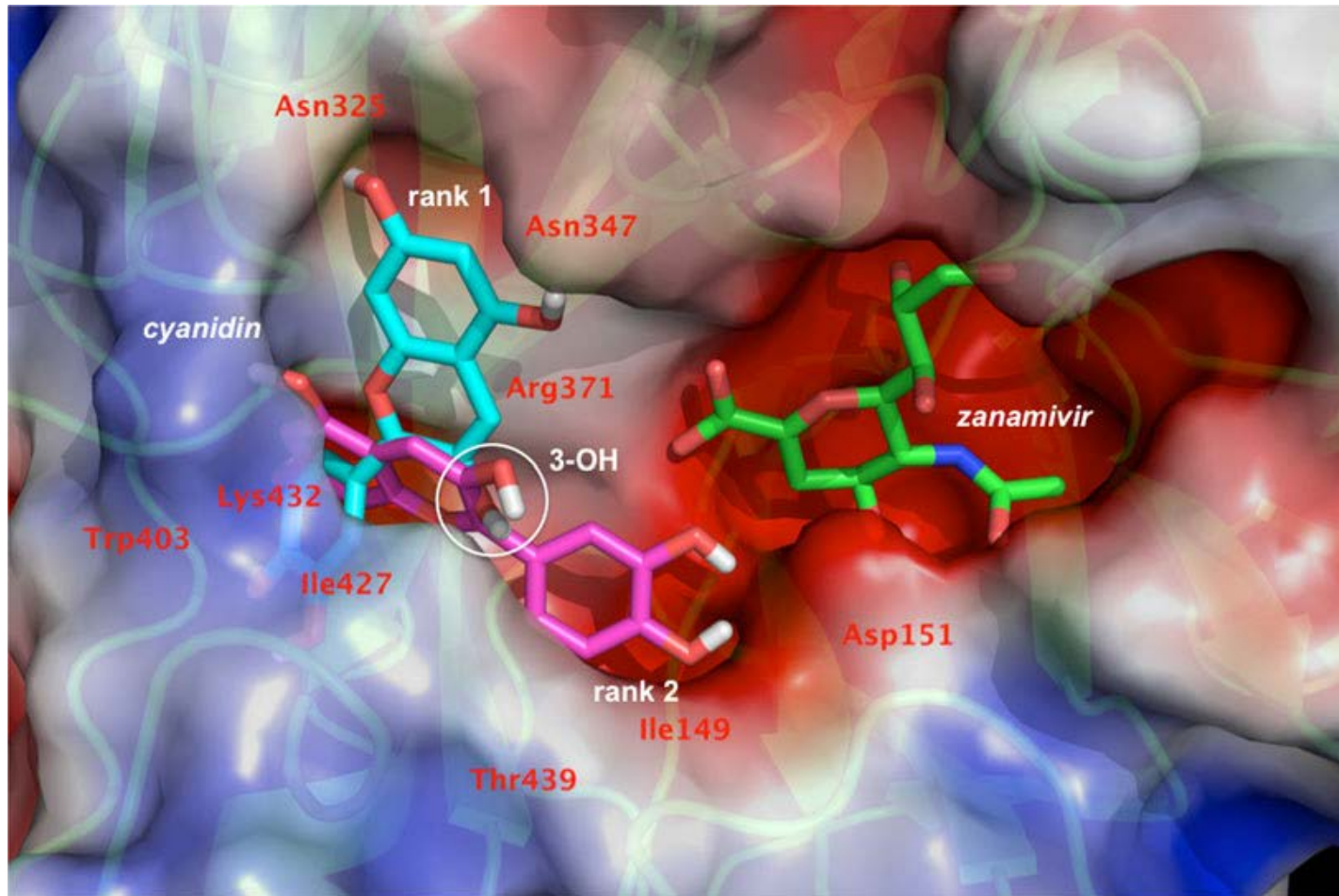
Black Elderberry: Literature

- Swaminathan K. **Binding of a natural anthocyanin inhibitor to influenza neuraminidase by mass spectrometry.** Anal Bioanal Chem. 2013;405(20) 6563-72
- Krawitz C. **Inhibitory activity of a standardized elderberry liquid extract against clinically-relevant human respiratory bacterial pathogens and Influenza A and B viruses.** 2011;25(11):16
- Barak V. **The effect of Sambucol, a black elderberry-based, natural product, on the production of human cytokines: I. inflammatory cytokines.** 2001;12(2): 290-6

Anthocyanin Binding and Inhibition of Influenza Neuraminidase

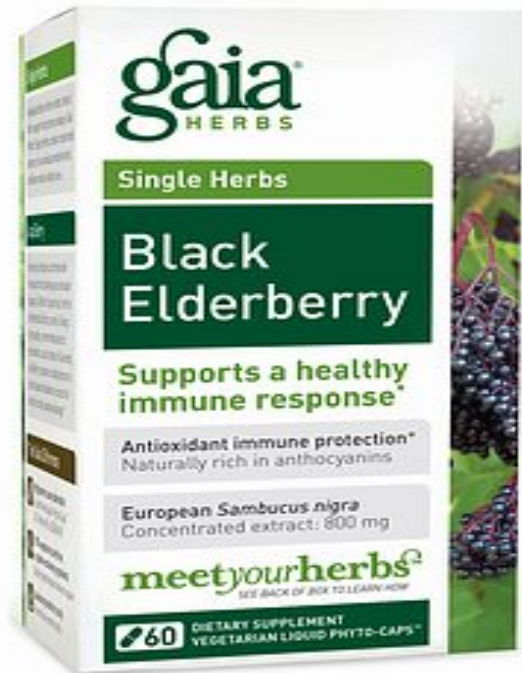
Anthocyanin (left) and zanamivir (right) docked onto the structure of influenza neuraminidase

Swaminathan 2013



Black Elderberry (Sambucus nigra)

One High Quality Extract



Directions

- Herbal dosing can be confusing based on whether crude herb, extract, standardization, etc.
- Can take equivalent of 3-5 grams of crude herb
4x daily
- Follow Label for *minimal* effective dosing

Sambucol™

Contains 3.8 g Black Elderberry Extract per 10 ml
Buy the “Original Formula” (center) Take Q.I.D.

THE ORIGINAL BLACK ELDERBERRY EXTRACT

Sambucol
BLACK ELDERBERRY
IMMUNE SYSTEM SUPPORT*

DIETARY SUPPLEMENT

Original Formula
Liquid

With 100% natural Sambucol® Black Elderberry Extract

Unique Extract

- Boosts immunity*
- Virologist developed
- Clinically tested

4 FL.OZ (120ML)

Sambucol
BLACK ELDERBERRY
IMMUNE SYSTEM SUPPORT*

DIETARY SUPPLEMENT

Forkids
Berry Flavored Liquid

With 100% natural Sambucol® Black Elderberry Extract

Unique Extract

- Boosts immunity*
- Virologist developed
- Clinically tested

4 FL.OZ (120ML)

Sambucol
BLACK ELDERBERRY
IMMUNE SYSTEM SUPPORT*

DIETARY SUPPLEMENT

Immune Formula
Liquid

With 100% natural Sambucol® Black Elderberry Extract

Unique Extract

- Boosts immunity*
- Virologist developed
- Clinically tested

4 FL.OZ (120ML)

Sambucol
BLACK ELDERBERRY
IMMUNE SYSTEM SUPPORT*

DIETARY SUPPLEMENT

COLD & FLU
NIGHT-TIME SYRUP

Relieves the symptoms of cold and flu while providing a peaceful night's sleep

Fast relief from:

- Sinus congestion
- Cough
- Aches & pains
- Fever & chills
- Sore throat
- Sleeplessness
- Headache

4 FL. OZ (120ML)

HOMEOPATHIC

Sambucol
BLACK ELDERBERRY
IMMUNE SYSTEM SUPPORT*

DIETARY SUPPLEMENT

Cold & Flu Relief

Fast relief from:

- Nasal & Sinus Congestion
- Runny Nose
- Sore Throat
- Coughing
- Sneezing
- Chills & Fever

Take at the first signs of cold & flu symptoms

4 FL. OZ (120ML)

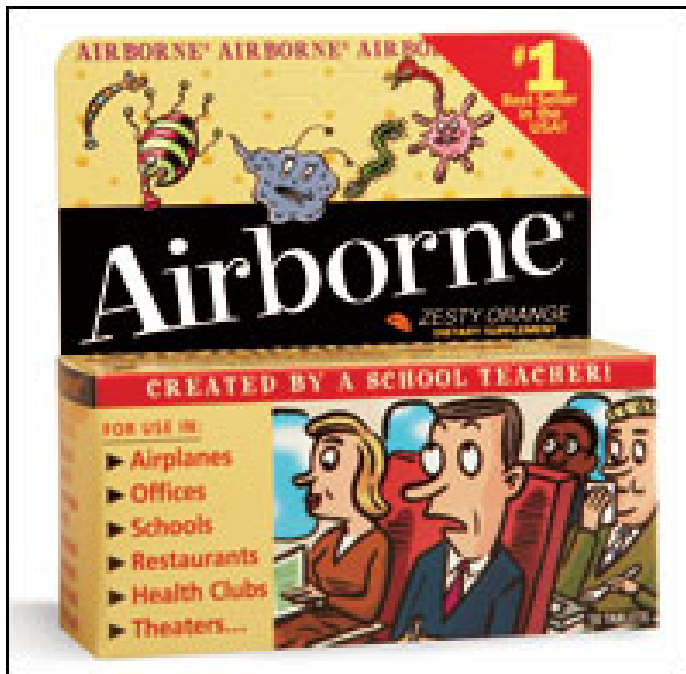
- The only Elderberry extract used in published clinical trials
- Recommended by Professionals
- Don't Be fooled by imitations!
- Ask for SAMBUCOL by name!

Sambucol IT!

Questionable Vitamin/Herbal products

- **No study** (or single study often by the manufacturer)
- Minimal or no **scientific plausibility**
- **Pseudo-scientific** extrapolations
- Minimal **meaningful clinical result**

Airborne™



- Mixture of many vitamins, amino acids (lysine and glutamine) and 7 herbs (in very low doses)
- **No clear evidence of efficacy**
- Perhaps helps those very deficient in the vitamins provided (C, Zn, Se)

Oscillococcinum TM



- Homeopathic remedy tested against influenza-like illness
- **17.1% vs. 10.3%** recovery w/in 48 hours*

*Ferley JP, et. al. **A controlled evaluation of a homeopathic preparation in the treatment of influenza-like syndromes.** Br J Clin Pharmacol. 1989;27:329-335

Case # 6: **“I am tired, burned-out,
stressed and depressed....”**

**“I do not want, or tolerate or need an
antidepressant.....”**

Lifestyle changes

Exercise

Therapist

What else?

Rhodiola rosea

Adaptogen (non-medical term)

...A substance that can act to increase an organism's resistance to physical, chemical and biological stressors

Long history of use in Eastern Europe and Asia for:

- Combating **stress-induced fatigue and depression ("burnout")**
- Improvement of mental performance

Rhodiola rosea

- Studies in humans and animals: **Some support for the claims made at doses of 340 or 680 mg. of an extract known as SHR-5**
- **Effects can be seen after single dose**
- **May reach maximal benefit in two weeks.**
- **No significant adverse effects reported** (*theoretical* risk of interaction with SSRI's)

Hung SK, Perry R, Ernst E. **The effectiveness and efficacy of rhodiola rosea L.: a systematic review of randomized clinical trials.** Phytomedicine. 2011;18(4): 235-244

Olsson EM et. al. **A randomised, double-blind, placebo-controlled, parallel-group study of the standardized extract shr-5 of the roots of Rhodiola rosea in the treatment of subjects with stress-related fatigue.** Planta med. 2009;75(2): 105-12

Darbinyan V et. al. **Clinical trial of Rhodiola rosea L. extract SHR-5 in the treatment of mild to moderate depression.** Nord J Psychiatry. 2007;61(5): 343-8

Rhodiola rosea

High Quality Manufacturers

NOW Foods



Gaia Herbs



For More Information: Look for these databases
(often linked to Electronic Medical Records)

1. **Natural Standard/ Natural Medicines Comprehensive Database**
2. **Micromedex/PDR** (becomes *AltMedDex*[®] when you type in a nutraceutical)

Today's *Prepared Agenda*:
An Introduction to Integrative Medicine with a focus on
the **Rational Use of Dietary Supplements**

1. A Rational Approach

- **Long Latency** vs. **Short Latency** deficiency syndromes
- Determining an **Optimal dose** —i.e. Vitamin D
- **Case #1--Daily Multivitamins** —helpful or harmful?
- Finding high **quality** supplements
- The herbal **“Entourage Effect”**

2. Useful Supplements for several common conditions

- **Case #2--Hyperlipidemia (Vit. D, Red Yeast Rice, Stanols/sterols, Nuts, DASH)**
- **Case #3--Hypertension (Mg+, Tomato extract, Mind-Body, Acupuncture)**
- **Case #4--URI's/ Influenza: “I always get sick” (Exercise, Quercetin, Green Tea)**
- **Case #5--URI's/ Influenza: “What can I take?” (Black Elderberry)**
- **Case #6—“I am tired, burned-out...stressed and depressed” (Rhodiola rosea)**

Thank You for Listening !

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