The Effect of a Fruit and Vegetable Mix on Hypertensive Subjects

Presented by John H Maher, D.C., D.C.C.N., F.A.A.I.M.
Co-Founder and V.P. of Education and Research BioPharma Scientific, San Diego, CA 92121

The following potential conflict of interest relationships are germane to my presentation:

**Product:** NanoGreens\textsuperscript{10}, Fruits and Vegetables to the Power of 10.

**Stock/Share Holder:** BioPharma Scientific, Inc. developer and manufacturer.

**Status of off-label use** of devices, drugs or other materials that constitute the subject of this presentation:

NanoGreens\textsuperscript{10} is a phytonutrient dietary supplement designed to provide the phytonutrition of up to 10 servings of fruits and vegetables a day. The findings reported herein have not been evaluated by the FDA. This product is not intended to diagnose, treat, cure or prevent any disease.
The Effect of a Fruit and Vegetable Mix on Hypertensive Subjects
Objectives

• To present data to support the hypothesis that the efficacy of the Dietary Approach to Stop Hypertension (DASH) diet is largely due to the phytonutrients found in fruits and vegetables.

• To encourage the investigation of the initial use of full spectrum fruit and vegetables phytonutrient dietary supplements in pre-hypertension and in combination with a prescription hypertension meds in Stage 1 and Stage 2 hypertension.
High Blood Pressure: The Silent Killer

• High blood pressure, the third leading cause of disability, has reached epidemic status globally.
• To quote the American Heart Association, high blood pressure is a ‘silent killer’ that "directly increases the risk of coronary heart disease and stroke".
• Indeed, high blood pressure may be causing 50 percent of all strokes and heart attacks!

Risks, Etiologies, Scope and Goals

• Mild elevations of blood pressure sustained over decades increases the risk of arteriosclerosis, stroke, myocardial infarction, heart and renal failure.

• Many different etiologies exist for hypertension including, but not limited to, metabolic syndrome, hypothyroidism, renal failure, alcoholism and adverse drug effects.

• The scope of this presentation is limited to non-complicated pre-hypertension and stage-one hypertension.

• The goals of therapy are to bring down into the optimal ranges and prevent the end-organ damage, especially to the heart, brain, eyes and kidneys.
New Developments in the Management of Hypertension

- Hypertension is the most common problem for which patients visit physicians.
- More than one half of all persons older than 65 years have hypertension, often isolated systolic hypertension.
- Improved control of hypertension has contributed to reductions of nearly 60% in stroke-related deaths, 53 % in deaths from ischemic heart disease since 1972.
- However, in the U.S., only 70% percent of patients with hypertension are aware of their condition, only 59% are receiving treatment, and only 34% have achieved adequate control.
- Recommendations to identify and treat hypertension are nearly universal.

New Developments in the Management of Hypertension

- *Isolated systolic blood pressure* elevation, the most common form of uncontrolled hypertension, is recognized as a significant risk factor for vascular complications in patients with hypertension.
- Some physicians accept inappropriately high blood pressure, especially systolic pressure, as adequate control in their patients.
- The new consensus is that persistent isolated elevation of systolic blood pressure should be treated to achieve a normal range (< 140 mm Hg), even in the presence of normal diastolic blood pressure.
- Evidence suggests that reduction of the blood pressure by 5 to 6 mm Hg can decrease the risk of stroke by 40%, of coronary heart disease by 15-20%, and reduces the likelihood of dementia, heart failure, and mortality from vascular disease.

- [http://www.aafp.org/afp/20030901/853.html](http://www.aafp.org/afp/20030901/853.html)
### Former BP Classifications


#### JNC-6 Classification of BP for Adults<sup>5</sup>

**Aged 18 Years and Older**

<table>
<thead>
<tr>
<th>Category</th>
<th>Systolic</th>
<th>Diastolic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal</td>
<td>&lt;120</td>
<td>&lt;80</td>
</tr>
<tr>
<td>Normal</td>
<td>&lt;130</td>
<td>&lt;85</td>
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<tr>
<td>High-normal</td>
<td>130-139</td>
<td>85-89</td>
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<tr>
<td>Hypertension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>140-159</td>
<td>90-99</td>
</tr>
<tr>
<td>Stage 2</td>
<td>160-179</td>
<td>100-109</td>
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<tr>
<td>Stage 3</td>
<td>≥ 180</td>
<td>≥ 110</td>
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# Risk Stratification and Treatment

<table>
<thead>
<tr>
<th>BP Stages (mmHg)</th>
<th>Risk Group A</th>
<th>Risk Group B</th>
<th>Risk Group C</th>
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<tr>
<td><strong>High-normal</strong></td>
<td>Lifestyle modification</td>
<td>Lifestyle modification</td>
<td>Drug Therapy†</td>
</tr>
<tr>
<td>(130-139 / 85-89)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Stage 1</strong></td>
<td>Lifestyle modification</td>
<td>Lifestyle modification</td>
<td>Drug Therapy</td>
</tr>
<tr>
<td>(140-159 / 90-99)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Stages 2 and 3</strong></td>
<td>Drug Therapy</td>
<td>Drug Therapy</td>
<td>Drug Therapy</td>
</tr>
<tr>
<td>(≥ 160 / ≥ 100)</td>
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* Lifestyle modification should be adjunctive therapy for all patients recommended for pharmacologic therapy.

** For patients with multiple risk factors, clinicians should consider drugs as initial therapy plus lifestyle modifications.

† TOD / CCD - target organ disease / clinical cardiovascular disease

†† For those with heart failure or renal insufficiency or those with diabetes
The National Heart, Lung, and Blood Institute classifies blood pressure as **normal, pre-hypertension, hypertension stages 1 & 2**.

**Normal blood pressure (BP)** is a systolic pressure of less than 120 mmHg and a diastolic pressure less than 80 mmHg (120/80 mmHg).

**Pre-hypertension** is when the systolic and/or diastolic blood pressure is higher than normal (120/80 mmHg) but not high enough to be considered high blood pressure (140/90 mm/Hg).

- Pre-hypertension is a systolic (top number) between 120 and 139 and/or a diastolic (bottom number) between 80 and 89.
- For example, blood pressure readings of 138/82, 128/70, or 115/86 are all in the "pre-hypertension" range.
• **Stage 1 hypertension** is a systolic pressure between 140 and 159 mm Hg and a diastolic pressure between 90 and 99 mm Hg or higher.

• **Stage 2 hypertension** is a systolic pressure of 160 mm Hg or higher, and a diastolic of 100 mm Hg or higher.

• *Both* increased systolic and diastolic blood pressures can increase the risk for congestive heart failure, heart attack, kidney disease, stroke, erectile dysfunction, amputation of the legs, and blindness.

• As people become older, the diastolic pressure will begin to decrease and the systolic blood pressure begins to increase, which may lead to high blood pressure. This disorder is called *isolated systolic hypertension*.
Stages of Hypertension and Treatment Strategies as Recommended by JNC 7

- **Pre-hypertension (120 to 139 / 80 to 89 mm Hg)**
  - Lifestyle modification (*diet, exercise, and weight reduction*)
  - Drug therapy in patients with diabetes mellitus or chronic kidney disease

- **Stage 1 (140 to 159 / 90 to 99 mm Hg)**
  - Consider coexisting conditions
  - Thiazide-type diuretics for most patients

- **Stage 2 (>=160 / >=100 mm Hg)**
  - Consider coexisting conditions
  - Two-drug combination for most patients

- **JNC = Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.**

New Developments in the Management of Hypertension
http://www.aafp.org/afp/20030901/853.html

• Nutritional management of hypertension has moved beyond simply restricting sodium intake to ensuring that patients consume adequate amounts of the major food groups, particularly those containing calcium, potassium, and magnesium...

• The mainstay of treatment remains a diuretic or a combination of a diuretic and either a beta blocker or an angiotensin-converting enzyme inhibitor...
American Family Physician Guidelines
http://www.aafp.org/afp/20030901/853.html

• When used alone, prescription anti-hypertensive medications average a BP reduction of 12/6.

• In patients requiring 20/10 reductions, two prescriptions are recommended.
Etiology

• Essential or primary hypertension: There is no accepted cause of essential hypertension which accounts for 90% of cases of HBP.

• However, there are risk factors that contribute to developing high blood pressure including:
  • salt intake, obesity, race, physical activity level.
  • heredity, diet, and stress level.

  http://www.naturalstandard.com/monographs/conditions/condition-highbloodpressure.asp?printversion=true
The Blood Vessel is the primary and central organ in HBP

• The vascular endothelium is the largest endocrine organ and the largest organ in the body.
• It is 14,000 sq. ft. in surface area, the size of 6 1/2 tennis courts in square area, and 5 times the heart size in mass with a total weight of about 2 kilograms.
• It is a metabolically active organ with endocrine, paracrine, autocrine and intracrine functions.
• The vascular endothelium under normal, healthy physiologic conditions forms a continuous sheet of organized monolayer polyhedral cells that becomes disorganized at extremes of hemodynamic shear stress (hypotension and hypertension).

Endothelial Dysfunction (ED)

- Endothelial dysfunction is a malfunction of the endothelium, the cells that line the inner surface of all blood vessels.

- Normal functions of endothelial cells include helping with coagulation, platelet adhesion, immune function, control of fluid and electrolyte content in and out of the cells.

- Endothelial dysfunction can result from high blood pressure. High blood pressure causes the blood vessels to become stiff and less able to constrict and dilate.

- Other causes include septic shock, hypercholesterolemia (high cholesterol), diabetes, and environmental factors such as cigarette smoking.

- Endothelial dysfunction is thought to be a key event in the development of atherosclerosis, leading to heart attacks.

ROS, ED and VSM

- Vascular biology plays a primary and pivotal role in the initiation and perpetuation of hypertension and subsequent target organ damage. (TOD)
- Endothelial dysfunction (ED), oxidative stress and vascular smooth muscle (VSM) dysfunction (hypertrophy, hyperplasia, remodeling) may be some of the first events that trigger essential hypertension.
- Nutrient-gene interactions determine specific phenotypic consequences of either vascular health, vascular disease or hypertension.

ROS and Antioxidants

- Hypertensive patients have an impaired endogenous and exogenous antioxidant defense mechanism. This includes elevated plasma malondialdehyde (MDA), hydrogen peroxide, $O_2$ production by PMNs and elevated NADPH oxidase,
- Reduced superoxide dismutase (SOD) in erythrocytes and PUFA on their membranes,
- Normal to low plasma selenium and low reduced glutathione peroxidase and nitric oxide (NO) levels,
- Low plasma vit. A, E and C, copper with increased zinc,
- More oxidative stress with more ROS produced and a greater than normal response to oxidative stress.
- Increased lipid peroxidation in serum and urine.

Nitrates and VSM

- Nitrates increase cyclic guanosine monophosphate (cGMP) levels in the vascular smooth muscle and reduce systemic blood pressure.
- Previous studies in subjects at risk for atherosclerosis have demonstrated arterial ED with reduced vasodilator responses after pharmacologic or physiologic stimulation of endothelial NO.
- Nitrate level per serving of green fruit and vegetable mix not yet determined.
Nitrates and VSM (cont.)

- Most have also shown a slight but non-significant impairment of vasodilatation in response to exogenous sources of NO, such as nitroglycerin (NTG).
- Interestingly, NTG responses were reduced in a large number of consecutively studied adults at risk for atherosclerosis, independent of any impaired endothelium-dependent responses.
- These findings are consistent with concomitant vascular smooth muscle dysfunction, independent of endothelial dysfunction.
Nitrates and VSM (cont.)

• Of concurrent interest, a small new study, published in the New England Journal of Medicine, suggests that the nitrates found in many vegetables may keep blood vessels healthy and lower blood pressure.

• Taking a daily dose of nitrate supplement equivalent to the amount normally found in 150 to 250 grams of a nitrate-rich vegetable -- such as spinach, lettuce, or beetroot -- for three days, resulted in an average diastolic blood pressure drop of 3.7 mm Hg.

• The researchers say these benefits are similar to those found among normotensive participants in the DASH trials and suggest that nitrate’s blood-pressure-lowering effects merit further study.
Dietary Relations

• A diet poor in fruits, vegetables, and whole grains and high in sodium (salt), high fat foods such as dairy (milk, cheese, sour cream), animal fat, and fried foods (potato chips, French fries, fried chicken) is associated with high cholesterol levels in the blood, which can lead to high blood pressure.

• Such a diet is also favors pro-oxidant processes, and may be low in phytonutrient antioxidants, have a poor Na/K ratio, be low in Mg and fiber, and high in pro-inflammatory fats.
DASH-1 and II

http://ana-jana.org/reprints/JANAHoustonSuppl.pdf p20

• **Dietary Approaches to Stop Hypertension**

• The DASH-I diet published in 1997 was a landmark nutritional trial in reducing blood pressure in hypertensive patients.

• The DASH-II sodium diet published in 2001 confirmed the value of DASH-I, but proved that moderate to severe sodium restriction further enhanced BP reduction.
DASH DIET Best

- A recent meta-analysis of clinical nutritional and lifestyle changes evaluated the effects of numerous interventions on systolic BP (Next Slide).
- The most effective intervention was the DASH diet followed by exercise, weight loss, sodium restriction and fish oil supplements.
- The least effective were increased intake of magnesium, calcium and potassium, or reduction in alcohol intake.
- This meta-analysis and other nutritional/diet studies emphasize the importance of the additive or synergistic effect of multiple nutrients, whole food and whole food concentrates with their nutrient combinations in a natural complex form to reduce BP and CVD.

Mark C. Houston, MD, SCH, FACP, FAHA, The Role of Vascular Biology, Nutrition, and Nutraceuticals in the Prevention and Treatment of Hypertension., JANA April 2002, Supplement No. 1 p. 18
# Lifestyle Changes and SBP Meta-analysis of Clinical Diet Trials

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Reduction in SBP (mmHg)</th>
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<tbody>
<tr>
<td>↑ Mg&lt;sup&gt;++&lt;/sup&gt;</td>
<td>0-1</td>
</tr>
<tr>
<td>↑ Ca&lt;sup&gt;++&lt;/sup&gt;</td>
<td>2</td>
</tr>
<tr>
<td>↑ K&lt;sup&gt;+&lt;/sup&gt;</td>
<td>4</td>
</tr>
<tr>
<td>↓ ETOH</td>
<td>4</td>
</tr>
<tr>
<td>Fish Oil</td>
<td>6</td>
</tr>
<tr>
<td>↓ Na&lt;sup&gt;+&lt;/sup&gt;</td>
<td>6</td>
</tr>
<tr>
<td>↓ Weight</td>
<td>8</td>
</tr>
<tr>
<td>Exercise</td>
<td>10</td>
</tr>
<tr>
<td>DASH diet</td>
<td>12</td>
</tr>
</tbody>
</table>
DASH-I : Trial Design

- **Selection criteria:**
  - Borderline or Stage-I hypertension (SBP < 160, DBP 80-95)
  - Age average 45 yrs; 2/3 minorities n=379.

- **Protocol: 3 Diets > C, F+V, Comb for 8 weeks**
  - Control diet x 3 weeks (C): Na = 3 gm / day, K+, Mg++, Ca++ = 25% U.S. average, Macronutrients = U.S. average (F + V 4 servings), Na+ / K+ Ratio = 1.7 Fiber = 9 gm / day
  - Control Diet Fruit + Vegetable Diet (F + V): Na+ = 3 gm / day, K+, Mg++, Ca++ = 75% U.S. average, F + V = 8.5 servings / day, Na+ / K+ Ratio = 0.7, Fiber = 31 gm / day
  - Combined Diet (Comb): Na+ = 3 gm/day, K+, Mg++, Ca++ = 75% U.S. average, F + V = 10 servings / day, Na+ / K+ Ratio = 0.6, Fiber > 31 gm / day, Low Fat Dairy = 2.7 servings/day,
Compliance & Misc. Results

- All diets were prepared and were well tolerated with a 93% adherence rate.
- There was no change in
  - alcohol intake,
  - weight, or
  - sodium excretion during the study.
DASH Results

Significant reductions in BP with controlled feeding and the described dietary modifications of increasing whole grains, nuts, poultry, fish, fruits, vegetables, K+, Mg++, and Ca++ while reducing intake of saturated and trans fatty acids, red meat, sweets, sugars and other refined carbohydrates.

The hypertensive subjects on the combined diet had the greatest BP reduction of 11.4/5.5 mm Hg.

Minority subjects, especially blacks, had greater reductions in BP compared to white subjects.

Hypertensive subjects had greater BP reductions than normotensive subjects.

Urinary Mg++ and K+ increased in the “F + V” and “C” groups, while urinary Ca++ decreased in the “F + V”.

The urinary Na+ remained constant in all three groups.
• The reduction in BP occurred immediately, reaching near maximum levels at two weeks, but was sustained throughout the eight-week study.

• In addition, the quality of life improved in subjects on the “F + V” and “C” diets.

• The combined treatment group had reductions in BP that were equal to that obtained with pharmacologic treatment of mild hypertension.

• DASH-I emphasizes the importance of combined nutrients as they occur in natural food.

• The DASH-II diet took the DASH-I diet one step further, proving that moderate to severe Na+ restriction reduced BP even more in all three study groups.
Summary of BP Reductions in DASH-I and DASH-II
Na\(^+\) Diets Hypertensive Patients and Overall

<table>
<thead>
<tr>
<th></th>
<th>SBP</th>
<th>DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>DASH-I Overall Combination Diet vs Control Diet</td>
<td>-5 mmHg</td>
<td>-3 mmHg</td>
</tr>
<tr>
<td>Dash I Hypertensive Pts. Comb. Diet vs Control Diet</td>
<td>-10.7 mmHg</td>
<td>-5.2 mmHg</td>
</tr>
<tr>
<td>DASH-II Overall Comb. Low Na(^+) DASH Diet vs vs. Control high Na(^+) Diet</td>
<td>-8.9 mmHg*</td>
<td>-4.5 mmHg*</td>
</tr>
<tr>
<td>DASH-II Hypertensive Pts. Comb. Low Na(^+) DASH Diet vs Control high Na(^+) Diet</td>
<td>-11.5 mmHg*</td>
<td>-6.8 mmHg*</td>
</tr>
</tbody>
</table>

* = p < 0.001
DASH-II Sodium Conclusions

- Reduction of sodium intake to 50 mmol/day from current recommendations of 100 mmol/day significantly reduces BP
- DASH combination diet with low sodium intake of 50 mmol/day lowers BP more in combination than either singly.
- Level of dietary sodium had twice BP reducing effect with the control diet than with DASH diet (p < 0.001)
- BP reductions occurred in all patients regardless of age, gender, ethnicity, or BP level (normals)
- Hypertensive patients, blacks and women had greatest BP reductions
- Low Na⁺ intake attenuated the hypotensive effects of K⁺ and Ca++
In 2004 the Journal of the American Dietary Association wrote, “when compared with the control diet, the DASH diet is higher in flavonols, flavanones, flavan-3-ols, beta-carotene, beta-cryptoxanthin, lycopene, lutein, zeaxanthin, and phytosterols...It therefore is possible that the health benefits of the DASH diet are partially attributable to the phytochemicals and might extend beyond cardiovascular disease risk reduction." The DASH study had established that a diet emphasizing fruits, vegetables, whole grains, poultry, fish and low-fat dairy products can reduce systolic blood pressure by an average of 5.5 mm Hg and diastolic blood pressure by 3 mm Hg.

- Most MM, Estimated phytochemical content of the dietary approaches to stop hypertension (DASH) diet is higher than in the Control Study Diet, J Am Diet Assoc. 2004 Nov;104(11):1725-7
“It had generally been thought that the effectiveness of the DASH diet was related to the high fiber, magnesium, potassium, folic acid and vitamin C content in this fruit and vegetable rich diet. Recent studies further suggest it may be that the plethora of phytonutrients in plant foods that bare a larger percent of the credit. For example, researchers in Israel found that a daily dose of tomato extract, standardized for 10% lycopene content, helped lower blood pressure in 31 men and women with moderately elevated blood pressure.”

D.A.S.H. and Phytonutrients (cont.)

- 20 naturally-occurring foods and specific compounds have angiotensin-converting enzyme inhibitor (ACEI) activity. Some of these substances appear to have ACEI activity comparable to that of commercially marketed pharmaceutical products.
- 11 naturally-occurring substances are noted to have calcium channel blocker activity,
- 11 diuretic activity,
- 11 enhance nitric oxide,
- 9 have angiotensin receptor-blocking properties,
- 16 direct vasodilator properties,
- 14 improve insulin sensitivity.
- Evidence for benefit is much stronger when multiple foods and nutraceuticals are considered together rather than as isolated components.
- “This summary provides a foundation for a rational, ‘stepped care’ or multi-dimensional nutritional and nutraceutical approach to the primary and secondary prevention of cardiovascular disease.”

Brent M. Egan, MD Professor of Pharmacology and Medicine at the Medical University of South Carolina, The Role of Vascular Biology, Nutrition, and Nutraceuticals in the Prevention and Treatment of Hypertension, JANA, April 2002 Supplement No. 1 p 1-2
• Combinations of natural phytonutrients in a balanced form appears to provide better antioxidant protection, BP and CVD reduction than single “bullet type” nutrient supplementation.

• Whole food concentrates of fruits, vegetables and fiber may provide additional nutrient value to the recommended eight to ten servings of fruits, vegetables and grains a day (about 400 grams/day) or ensure better nutrition in the form of an “insurance policy” when dietary intake is suboptimal for a variety of reasons.

• Several prospective clinical human trials have been published or are in progress on such a product. These studies in humans have shown significant increases in serum and lymphocyte antioxidant and vitamin levels following oral ingestion, reduced oxidative stress, weight reduction with increased lean body mass and reduced total body fat, improved cellular immune function in lymphocytes, reduced DNA damage in lymphocytes, improved brachial artery flow-mediated vasodilation and improved endothelial function, improved arterial compliance, reduction in homocysteine and BP.
Flavonoids

- Over 4,000 naturally occurring flavonoids have been identified in such diverse substances as fruits, vegetables, red wine, tea, soy and licorice.
- Flavonoids (flavonols, flavones and isoflavones) are potent free radical scavengers that inhibit lipid peroxidation, prevent atherosclerosis, promote vascular relaxation and have antihypertensive properties.
- In addition, they reduce stroke, and provide cardio-protective effects that reduce CHD morbidity and mortality in the Zutphen Elderly Study, Finnish Study and U.S. Health Professionals Study.

Lycopene Carotenoid

- Lycopene is a non-provitamin-A carotenoid, potent antioxidant found in tomatoes and tomato products, guava, pink grapefruit, watermelon, apricots, and papaya in high concentrations.
- Lycopene has recently been shown to produce a significant reduction in BP, serum lipids and oxidative stress markers.
- 30 subjects with Grade I hypertension, age 40-65, taking no antihypertensive or anti-lipid medications treated with a tomato lycopene extract for eight weeks.
  - The SBP was reduced from 144 to 135 mm Hg (9 mm Hg reduction), and DBP fell from 91 to 84 mm Hg (7 mm Hg reduction) $p < 0.01$.
- A similar study of 35 subjects with Grade I hypertension showed similar results on SBP, but not DBP. Serum lipids were significantly improved in both studies without change in serum homocysteine.

Green and Black Tea

- Tea contains many active compounds that may alter BP, including flavonoids, which are polyphenolic compounds with vasodilatory and antioxidant effects, theanine, theobromine, quercetin, epigallocatechin-3-0-gallate (EGCG), gamma-glutamylmethylamide (GMA), thearubigins and theaflavins.

- Additional studies in humans will be required to accurately assess these BP effects.

Chlorella and Guava Fruit

• **Chlorella**: 24 hypertensive patients given 10 gm of chlorella tablets and 100 ml of chlorella extract per day had no significant mean change in BP. However, a small subgroup of six patients had a reduction in DBP from 96.5 mm Hg to < 90 mm Hg. *Effects on ED, SNS or the replacement of K+, Mg++, Ca++ and fiber may account for the antihypertensive effect.*

• **Guava Fruit**: 72 patients with essential hypertension treated with 0.5 to 1.0 kg of guava fruit daily for four weeks in a randomized, single-blind, placebo-controlled trial. The patients receiving guava had a net decrease in mean BP of 7.5/8.5 mm Hg (p < 0.05). *The high content of soluble fiber and potassium may account for the BP lowering.*

Summary

Vascular biology (ED and VSM dysfunction) plays a primary role in the initiation and perpetuation of hypertension, CVD, and TOD. (Target Organ Damage)

Nutrient-gene interactions are a predominant factor in promoting beneficial or detrimental effects in cardiovascular health and hypertension.

Nutrition (natural whole food, nutraceuticals) can prevent, control and treat hypertension through numerous vascular biology mechanisms.

Oxidative stress initiates and propagates hypertension and cardiovascular disease.

Antioxidants may prevent and treat hypertension.
Summary (cont.) p 47

• Whole food and whole food concentrates of fruits, vegetables and fiber with natural combinations of balanced phytonutrients, phytochemicals, antioxidants, vitamins, minerals and appropriate macronutrients and micronutrients are generally superior to single component or isolated artificial or single component natural substances for the prevention and treatment of hypertension and CVD.

• However, there is a role for the selected use of single and component nutraceuticals, vitamins, antioxidants and minerals in the treatment of hypertension based on scientifically controlled studies as a complement to optimal nutritional, dietary intake from food and other lifestyle modifications.

• Exercise, weight reduction, smoking cessation, and alcohol and caffeine restriction, as well as other changes in lifestyle must be incorporated.
Dr Houston’s “Recommendations”

1. DASH I and DASH II-Na+ diets
2. Sodium restriction ...........................................50 – 100 mmol
3. Potassium ..................................................60 – 100 mEq
4. Potassium/sodium ratio ..................................> 5:1
5. Magnesium ...............................................500 – 1000 mg
6. Calcium .....................................................1000 – 1500 mg
7. Zinc ............................................................25 mg
8. **Protein**: total intake (40% total calories). 10 – 1.5 mg/kg
   • A. Non-animal sources preferred but lean or wild animal protein in moderation
   • B. Hydrolyzed whey protein ........................5 grams
   • C. Soy protein (fermented is best) .................30 grams
   • D. Hydrolyzed wheat germ isolate ..............2 – 4 grams
   • E. Sardine muscle concentrate extract ..........3 mg
   • F. Cold water fish, fowl poultry
9. **Fats**: 25% total calories
   • A. Omega-3 fatty acids (30%) PUFA ......3 – 4 grams (DHA, EPA, ALA, cold water fish)
   • B. Omega-6 fatty acids (10%) PUFA (flax, CLA, canola oil, nuts)
<table>
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<tr>
<th>Supplement</th>
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<td>Vitamin E</td>
<td>400 to 800 IU QD</td>
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<td>Vitamin B-6</td>
<td>100 mg QD to BID</td>
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<td>Co-enzyme Q-10 (QGEL®)</td>
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<tr>
<td>Lipoic Acid</td>
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<td>L-Carnitine</td>
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<td>Taurine</td>
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<tr>
<td>Σ NADA</td>
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Compliance?

- While these are very thorough recommendations, and I am not presuming that Dr. Houston is suggesting someone do all these things, nonetheless experience suggests that compliance may be a problem in a significant percentage of patients.
- And how to figure which patient needs what most?
The Logan Study- The Effect of Fruit and Vegetable Powder Mix on Hypertensive Subjects


- The Logan Chiropractic research was designed to study the effects of a green phytonutrient-rich fruit and vegetable powder mix on cardiovascular health, including blood pressure, in forty subjects, half of which were controls.

- This green fruit and vegetable powder consisted of micro algae (spirulina, chlorella, Dunaliella salina), barley grass juice powder, multiple fruit and vegetable powders of all the colors, lecithin, acerola cherry, fermented cabbage, milk thistle, plant enzymes, quinoa sprout, lemon peel, oat beta glucan, soluble rice bran, concentrated extracts of green and white tea, resveratrol, lutein, zeaxanthin, lycopene, cinnamon, raspberry, iso quercitin-rutin 50/50 and aloe vera.

- The product was formulated with a liposomal nanotechnology to enhance the bioavailability of the lipophillic phytonutrients.

- Naturally flavored to enhance compliance.
One serving of a 12 g scoop mixed in 6-8 ounces of water supplied:

• 50 calories, 1.5 g fat, 24 mg NA, 152 mg K, 8 gm carbohydrates, less than 1 gm fiber, 2 gm protein,

• providing 50 % RDV of Vitamin A as beta-carotene, 50% Vitamin C from acerola cherry, 11% choline from lecithin.

• All other measured vitamins and minerals were under 4% RDV per 12 g serving.

• The product had an oxygen radical absorbance capacity (ORAC) capacity of 583 per gram, or 6,996 ORAC units per serving.

• Subjects were given 1 scoop (12 gm) B.I.D.
Selection Criteria

• Selection criteria were similar to DASH diet.
• Mild hypertension, otherwise healthy
• No medications
• Student and teacher population
• Subjects were given 2 scoops a day (total 24 gm) to mix with water to taste (6 - 12 ounces).
• Supplementation was continued 90 days.
Logan Study Results

• After taking the supplement for 90 days, both the systolic and diastolic blood pressure decreased significantly.

• On average, the systolic blood pressure decreased **12.4 mm HG** (140.4±17.7 mm Hg to 128±14.2 mm Hg) and the diastolic blood pressure decreased **7.1 mm Hg** (90.2±7.7 mm Hg to 83.1±7.4 mm Hg).

• No significant blood pressure decrease was observed in the control group. It was observed that taking the green phytonutrient-rich fruit and vegetable drink for 90 days significantly reduced blood pressure.

Nutritional Analysis NG10

REPORT OF ANALYSIS

SAMPLE NUMBER: 50700410
BATCH NUMBER: 50700410
DATE ENTERED: 07/05/05
REPORT PRINTED: 05/25/07

ALISON CALHOUN
BIOPHARMA SCIENTIFIC, INCORPORATED
6350 NANCY RIDGE DRIVE, SUITE 103
SAN DIEGO, CA 92121

NANO GREENS: LOT #001.1

PURCHASE ORDER NUMBER: 0090/CHARGE - VISA

SERVING SIZE = 12.05 GM

<table>
<thead>
<tr>
<th>Assay</th>
<th>Content/100 GM</th>
<th>Per Serving</th>
<th>% DV / Serving</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories</td>
<td>423.0</td>
<td>51.0</td>
<td></td>
</tr>
<tr>
<td>Calories from Fat</td>
<td>99.0</td>
<td>11.9</td>
<td></td>
</tr>
<tr>
<td>Saturated Fat</td>
<td>2.77</td>
<td>0.334</td>
<td>1.67</td>
</tr>
<tr>
<td>Calculated as Acids</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sum of Quantitated Fatty Acids</td>
<td>11.0</td>
<td>1.33</td>
<td>2.04</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>&lt; 1.0</td>
<td>MG</td>
<td></td>
</tr>
<tr>
<td>Sodium</td>
<td>202.0</td>
<td>24.34</td>
<td>1.01</td>
</tr>
<tr>
<td>Potassium</td>
<td>1260.0</td>
<td>151.83</td>
<td>4.34</td>
</tr>
<tr>
<td>Total Carbohydrate</td>
<td>70.0</td>
<td>8.44</td>
<td>2.81</td>
</tr>
<tr>
<td>Dietary Fiber</td>
<td>3.6</td>
<td>.43</td>
<td>1.74</td>
</tr>
<tr>
<td>Sugar Profile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fructose by HPLC</td>
<td>1.8</td>
<td>.22</td>
<td></td>
</tr>
<tr>
<td>Glucose by HPLC</td>
<td>9.2</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Sucrose by HPLC</td>
<td>2.1</td>
<td>.25</td>
<td></td>
</tr>
<tr>
<td>Maltose by HPLC</td>
<td>10.1</td>
<td>1.22</td>
<td></td>
</tr>
</tbody>
</table>
SAMPLE NUMBER: 50700410
NANO GREENS: LOT #001.1

<table>
<thead>
<tr>
<th>Assay</th>
<th>Content/100 GM</th>
<th>Per Serving</th>
<th>% DV / Serving</th>
</tr>
</thead>
<tbody>
<tr>
<td>LACTOSE</td>
<td>&lt; 0.1 GM</td>
<td>2.80 GM</td>
<td></td>
</tr>
<tr>
<td>TOTAL SUGAR</td>
<td>23.2 GM</td>
<td>1.31 GM</td>
<td></td>
</tr>
<tr>
<td>PROTEIN (N X 6.25) DUMAS METHOD</td>
<td>10.9 MG</td>
<td>1.64 MG</td>
<td></td>
</tr>
<tr>
<td>BETA CAROTENE BY HPLC</td>
<td>13.6 MG</td>
<td>1.64 MG</td>
<td></td>
</tr>
<tr>
<td>VITAMIN A FROM CAROTENE</td>
<td>22700 IU</td>
<td>2735.4 IU</td>
<td>54.71</td>
</tr>
<tr>
<td>VITAMIN C</td>
<td>302. MG</td>
<td>36.4 MG</td>
<td>60.65</td>
</tr>
<tr>
<td>CALCIUM</td>
<td>304.0 MG</td>
<td>36.63 MG</td>
<td>3.66</td>
</tr>
<tr>
<td>IRON</td>
<td>5.72 MG</td>
<td>0.689 MG</td>
<td>3.83</td>
</tr>
<tr>
<td>VITAMIN K</td>
<td>33.4 MCG</td>
<td>4.02 MCG</td>
<td>5.03</td>
</tr>
<tr>
<td>FOLIC ACID</td>
<td>150. MCG</td>
<td>18.1 MCG</td>
<td>4.52</td>
</tr>
<tr>
<td>MAGNESIUM</td>
<td>133.0 MG</td>
<td>16.03 MG</td>
<td>4.01</td>
</tr>
<tr>
<td>MOISTURE (100 DEGREE VAC. OVEN)</td>
<td>3.4 GM</td>
<td>0.41 GM</td>
<td></td>
</tr>
<tr>
<td>ASH</td>
<td>4.7 GM</td>
<td>0.57 GM</td>
<td></td>
</tr>
<tr>
<td>FATTY ACID AND TRANS FAT BY GC</td>
<td>0.029 GM</td>
<td>0.0035 GM</td>
<td></td>
</tr>
<tr>
<td>TOTAL TRANS FATTY ACIDS</td>
<td>0.029 GM</td>
<td>0.0035 GM</td>
<td></td>
</tr>
<tr>
<td>MONounsaturated Fat</td>
<td>1.86 GM</td>
<td>0.224 GM</td>
<td></td>
</tr>
<tr>
<td>POLYunsaturated Fat</td>
<td>5.87 GM</td>
<td>0.707 GM</td>
<td></td>
</tr>
</tbody>
</table>

*SIGNED*  
DATE 05/25/07

BY AND FOR COVANCE LABORATORIES INC.
Ingredients NG10

• Greens Blend (Proprietary) 2350 mg: Barley Grass Juice Powder*, Spirulina*, Chlorella (Japanese soft shell)
• Phyto-Nutrient Blend (Proprietary) 325 mg: Blueberry, Green Tea Extract, Grape Seed Extract, Cranberry, Raspberry, Tart Cherry, Pine Bark Extract, Broccoli, Tomato, Carrot, Spinach, Kale, Brussels Sprout, Bilberry, Elderberry, Pomegranate, Blackberry
• Iso-quercitin/Rutin 50/50: 160 mg
• Raspberry Extract (20% Ellagic Acid): 50 mg
• Fruit & Vegetable Blend (Proprietary; freeze-dried, low temp dried) 900 mg: Apple*, Carrot*, Mango*, Sweet Potato*, Lemon*, Parsley*, Peach*, Kale*, Broccoli*, Spinach*, Leek*, Beet*, Cranberry* (Quinic Acid 6%)
• Acerola Cherry Powder* (17.5% Ascorbic Acid): 175 mg
• Rice Bran Soluble*: 2500 mg
• Aloe Vera Powder Extract* (100:1 freeze dried): 30 mg
• Green Tea, White Tea (decaffeinated, 50% Polyphenol): 100 mg
• Polygonum Cuspidatum (15% Resveratrol): 50 mg
• Oat Beta Glucan*: 2200 mg
• Cinnamon Blend (Proprietary): 50 mg Cinnamon Extract 8%, Cinnamon Bark Powder*
• Milk Thistle (20% Silymarin): 50 mg
• Marigold Extract (5% Lutein with Zeaxanthin) 50 mg
• Dunaliella Salina (Natural Carotenoids) 100 mg
• Enzymes (plant-based)40 mg: Alpha Amylase, Bromelain, Cellulase, Galactosidase, Glucoamylase, Hemicellulase, Lipase, Papain, Protease
• Lecithin (from non GMO soy): 1925 mg
• Cabbage (Japanese, fermented) 30 mg
• Lycopene Extract-10% (from tomato)25 mg
• Lemon Peel Powder* 25 mg
• Quinoa Sprout*90 mg
• Artichoke Extract (5% Cynarin)20 mg
• Atlantic Kelp Powder* (Laminara Digitata)20 mg
* certified organic
# The Cytotoxic Reactive Oxygen Species and the Natural Defense Mechanisms

<table>
<thead>
<tr>
<th>Reactive Oxygen Species</th>
<th>Antioxidant Defense Mechanisms</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Free Radicals</strong></td>
<td></td>
</tr>
<tr>
<td>( \text{O}_2 \cdot )</td>
<td>Superoxide anion radical</td>
</tr>
<tr>
<td>( \text{OH} \cdot )</td>
<td>Hydroxyl radical</td>
</tr>
<tr>
<td>( \text{ROO} \cdot )</td>
<td>Lipid peroxide (peroxyl)</td>
</tr>
<tr>
<td>( \text{RO} \cdot )</td>
<td>Alkoxy radical</td>
</tr>
<tr>
<td>( \text{RS} \cdot )</td>
<td>Thiyl</td>
</tr>
<tr>
<td>( \text{NO} \cdot )</td>
<td>Nitric oxide</td>
</tr>
<tr>
<td>( \text{NO}_2 \cdot )</td>
<td>Nitrogen dioxide</td>
</tr>
<tr>
<td>( \text{ONOO} \cdot )</td>
<td>Peroxynitrite</td>
</tr>
<tr>
<td>( \text{CCl}_3 \cdot )</td>
<td>Trichloromethyl</td>
</tr>
<tr>
<td>( \text{H}_2\text{O}_2 )</td>
<td>Hydrogen peroxide</td>
</tr>
<tr>
<td>( \text{HOCl} )</td>
<td>Hypochlorous acid</td>
</tr>
<tr>
<td>( \text{ONOO} \cdot )</td>
<td>Peroxynitrite</td>
</tr>
<tr>
<td>( ^1\text{O}_2 )</td>
<td>Singlet oxygen</td>
</tr>
</tbody>
</table>

| **Enzymatic Scavengers** |                                |
|                         | SOD Superoxide dismutase       |
|                         | \( 2\text{O}_2 \cdot + 2\text{H}^+ \rightarrow \text{H}_2\text{O}_2 + \text{O}_2 \) |
|                         | CAT Catalase (peroxisomal-bound) |
|                         | \( 2\text{H}_2\text{O}_2 \rightarrow \text{O}_2 + \text{H}_2\text{O} \) |
|                         | GTP Glutathione peroxidase     |
|                         | \( 2\text{GSH} + \text{H}_2\text{O}_2 \rightarrow \text{GSSG} + 2\text{H}_2\text{O} \) |
|                         | \( 2\text{GSH} + \text{ROOH} \rightarrow \text{GSSG} + \text{ROH} + 2\text{H}_2\text{O} \) |

| **Nonenzymatic scavengers** |                                |
|                            | Vitamin A                      |
|                            | Vitamin C (ascorbic acid)      |
|                            | Vitamin E (\( \alpha \)-tocopherol) |
|                            | \( \beta \)-carotene           |
|                            | Cysteine                       |
|                            | Coenzyme Q                     |
|                            | Uric Acid                      |
|                            | Flavonoids                     |
|                            | Sulphhydryl group              |
|                            | Thioether compounds            |

The superscripted bold dot indicates an unpaired electron and the negative charge indicates a gained electron. \( \text{GSH} \), reduced glutathione; \( \text{GSSG} \), oxidized glutathione; \( \text{R} \), lipid chain. Singlet oxygen is an unstable molecule due to the two electrons present in its outer orbit spinning in opposite directions.
# Report for BioPharma Scientific

<table>
<thead>
<tr>
<th>Sample ID</th>
<th>Brunswick Lab ID</th>
<th>ORAC\textsubscript{hydro}* (μmole TE/g)</th>
<th>ORAC\textsubscript{lipid}^\wedge (μmole TE/g)</th>
<th>ORAC\textsubscript{total} (μmole TE/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nanogreens 10</td>
<td>07-1121</td>
<td>559</td>
<td>129</td>
<td>688</td>
</tr>
<tr>
<td>Lot # 061497</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The ORAC analysis provides a measure of the scavenging capacity of antioxidants against the peroxyl radical, which is one of the most common reactive oxygen species (ROS) found in the body. ORAC\textsubscript{hydro} reflects water-soluble antioxidant capacity and the ORAC\textsubscript{lipid} is the lipid soluble antioxidant capacity. Trolox, a water-soluble Vitamin E analog, is used as the calibration standard and the ORAC result is expressed as micromole Trolox equivalent (TE) per gram. The acceptable precision of the ORAC assay is 15% relative standard deviation.\textsuperscript{1-23}

<table>
<thead>
<tr>
<th>Sample ID</th>
<th>Brunswick Lab ID</th>
<th>HORAC* (μmole CAE/g)</th>
<th>NORAC^ (μmole TE/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nanogreens 10</td>
<td>07-1121</td>
<td>39</td>
<td>63</td>
</tr>
<tr>
<td>Lot # 061497</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Caffeic Acid is used as the calibration standard and the HORAC result is expressed as μmole Caffeic Acid equivalent (CAE) per gram.

^Trolox is used as the calibration standard and the NORAC result is expressed as μmole Trolox equivalent (TE) per gram.

Sample was received in an unopened canister with a heat induction seal.

Testing performed by J. Frietas and J. Theobald.

Approved by: [Signature]
Boxin Ou, PhD.

B-5830 / 4-16-07 lrh

Samples will be discarded one month from report date, unless otherwise notified by customer in writing.

\textsuperscript{1} Ou, B.; Hampsch-Woodill, M.; Prior, R. L.; Development and Validation of an Improved Oxygen Radical Absorbance Capacity Assay using Fluorescein as the Fluorescent Probe. Journal of Agricultural and Food Chemistry.; 2001; 49(10); 4619-4626


Differing Antioxidant Activities


Four Top Selling Phytonutrient Powders

<table>
<thead>
<tr>
<th>Category</th>
<th>Antioxidant Capacity (umole TE/gram)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Professional #1</td>
<td>25,000</td>
</tr>
<tr>
<td>Professional #2</td>
<td>10,000</td>
</tr>
<tr>
<td>Retail</td>
<td>5,000</td>
</tr>
<tr>
<td>MLM</td>
<td>2,000</td>
</tr>
</tbody>
</table>
NanoSorb™ Liposome

- Polar Lipids (Phospholipid)
- Lipid Soluble ingredients (Drugs, Nutrients & vitamins)
- Water Soluble ingredients (Drugs, Nutrients & vitamins)
- H₂O Layer
- Lipid Layer
In Vivo Bioavailability of Liposome Encapsulated Phytonutrients

Pre & Post In Vivo Plasma Antioxidant

Antioxidants in Plasma

- Before taking product
- 1 week after taking product
- 3 weeks after taking product

*In VIVO Plasma Results After Supplementation of 1 g/day of Phytonutrient Concentrate Ingredient Utilizing Liposomes
An investigation of antioxidant and triglyceride status of rats consuming a diet enriched by a complex phytonutrient supplement, NanoGreens\textsuperscript{10}

The aim of the study:

This investigation examined the influence of a complex phytonutrient supplement (NG\textsuperscript{10}) on total antioxidant capacity (TAC), endogenous antioxidant enzyme activity (SOD), and triglyceride concentration in laboratory animals.

- Poster Presentation “Functional Food in Europe - International Developments in Science and Health Claims” on May 9-11, 2007, Malta
  - Alexander S. Krylov\textsuperscript{1}, Marina V. Ivanova\textsuperscript{2}, Constantine B. Shumaev\textsuperscript{2}, Galina G. Konovalova\textsuperscript{2}
  - 1- Institute of General Pathology and Pathophysiology, Russian Academy of Medical Sciences, Baltijskaya, Moscow, Russia
  - 2 - Cardiology Research Center, Ministry of Health, Cherepkovskaya 15A, Moscow, Russia
Animal Study NG$^{10}$ TAC

Total antioxidant status

Days

NanoGreens/Control

Days
S.O.D. Liver

SOD activity in liver

Units/mg protein

<table>
<thead>
<tr>
<th>Days</th>
<th>Control</th>
<th>NanoGreens</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>42</td>
<td>*</td>
<td></td>
</tr>
</tbody>
</table>

Legend:
- Red: Control
- Green: NanoGreens
Triglycerides in Plasma

![Graph showing the change in triglycerides in plasma over days, with NanoGreens/Control compared to control.](image-url)
Conclusion

• A dietary supplement providing many of the phytonutrients /antioxidants of up to 10 servings of fruits and vegetables of all the colors, but significantly lower in fiber, vitamins and minerals, nonetheless mimicked the results of the DASH II diet, without concomitant sodium restriction.

• This study supports the hypothesis that it is the phytonutrients in fruits and vegetables that are the major factor in the proven efficacy of the DASH diet.

• If these findings can be replicated, then such supplementation may be considered among the primary choices in initial and supportive non-pharmacological interventions in optimizing blood pressure.
Discussion

This study also reinforces the consensus opinion that that the benefit is much stronger when the phytonutrition of multiple fruits and vegetables are considered together rather than when consumed as isolated nutrients.

It should be noted that the size of the study was small (20 subjects/ 20 controls). There was no placebo used. Further testing on a larger base is warranted to confirm results.

Such studies are currently on going at University of Miami. Although a healthy diet rich in fruits and vegetables has no peer in overall benefits, compliance hurdles in strict dietary regimes is a familiar obstacle to all clinicians.

Therefore green phytonutrient-rich fruit and vegetable powders similar in formula and dosage to the one in the Logan Study may indeed be worthy of further clinical investigation.
Stevia Effect

• Natural Standards Grading* for Stevia
• Grade B: Hypertension (Ranks with Co Q10)
• Grade B: Hyperglycemia
• Adult Dosing Hypertension: 250-500mg orally TID.
• NG10 has 200 mg / scoop.

* Key to grades: A: Strong scientific evidence for this use; B: Good scientific evidence for this use; C: Unclear scientific evidence for this use; D: Fair scientific evidence against this use (it may not work); F: Strong scientific evidence against this use (it likely does not work).

Stevia Effect

• The inclusion of stevia weakens this presentations hypothesis as it is a plant phyto-chemical not expected in the D.A.S.H. diet.

• Stevia is included to enhance taste, and therefore compliance, in consuming 24 gm a day in water as compared to glycemic juices.

• However, as to clinically utility in hypertension, and the often related hyperglycemia, stevia seems well indicated.
Considerations

• What is the exact dose and dose-frequency of these agents that will allow clinical benefit?

• How homogeneous is the production of these products so that their bioavailability can be assured?

• These are just a few issues that will need to be carefully evaluated in clinical hypertension trials before these agents are widely endorsed by the practicing community.

• Jan Basile, MD, Associate Professor of Medicine, Ralph H. Johnson VA Medical Center, Division of General Internal Medicine/Geriatrics, Medical University of South Carolina. "Nutraceuticals and Vascular Biology: Are They Ready For Prime Time Use?" JANA April 2002, Supplement No. 1 p.3-4
Closing Remarks

• No requirement to prove purity exists for dietary supplements sold in pharmacies, health food stores and supermarkets in the United States.

• During the past 10 years, however, dietary supplements have been reported to have fewer and less serious side effects than prescription drugs, conservatively estimated to be 100,000 deaths per year.

• Certified, high quality supplements with standardized ingredients that are bioavailable and potent with 100% purity, no toxicity or adverse effects and have accurate labeling and expiration dates should be sought by the wise consumer.

• The terms “all natural”, “organic”, “herbal”, etc., do not necessarily imply potency, purity, safety, or efficacy.
Closing Remarks

• Health professionals should look for phytonutrient products that have:
• Antioxidant testing, *in vivo* and *in vitro*
• Heavy metal and microbial analysis
• Nutritional analysis
• Animal and human studies, completed and ongoing.
Natural Standard is an international research collaboration that aggregates and synthesizes data on complementary and alternative therapies. Using a comprehensive methodology and reproducible grading scales, information is created that is evidence-based, consensus-based, and peer-reviewed, tapping into the collective expertise of a multidisciplinary Editorial Board. The mission of this collaboration is to provide objective, reliable information that aids clinicians, patients, and healthcare institutions to make more informed and safer therapeutic decisions. Natural Standard is widely recognized as one of the world’s premier sources of information in this area. For more information, please contact us.

http://www.naturalstandard.com/monographs/conditions/condition-highbloodpressure.asp?printversion=true
Contact Information

• Dr John H Maher
• jmaher@biopharmasci.com
• 858-622-9493 x 220
• www.biopharmasci.com
• www.biopharmasci.com/hp/sng/science.asp
• www.biopharmasci.com/hp/sng/analysis.asp