THE EFFECT OF A FRUIT AND VEGETABLE MIX ON HYPERTENSIVE SUBJECTS AND ITS POTENTIAL AS A HIGH COMPLIANCE ALTERNATIVE TO THE D.A.S.H DIET

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ABSTRACT

High blood pressure has such severe morbidity that it has been dubbed "*The Silent Killer*". Primary hypertension is considered to be an expression of a pathophysiological condition of the vascular system. Over the last decade, the lifestyle and pharmacological treatment recommendations and goals have become more aggressive. The dietary modification called the "Dietary Approach to Stop Hypertension" a.k.a the DASH diet has been shown to significantly lower both systolic and diastolic blood pressure. Recent studies suggest that many nutraceuticals have potentially salubrious effects on hypertension. A pilot study was conducted at Logan College using a fruit and vegetable green powder mix drink that purported to provide levels of phytochemicals similar to the DASH diet. Results on blood pressure reduction displayed similar efficacy as the DASH diet. Considering the compliance hurdles implicit in the DASH diet, it is suggested that clinical investigation in the use of such phytochemical rich fruit and vegetable powders may be a reasonable science-based alternative treatment option for the physician.

INTRODUCTION

High blood pressure has such severe morbidity that it has been dubbed "*The Silent Killer*". Primary hypertension is considered to be an expression of a pathophysiological condition of the vascular system. Over the last decade, the lifestyle and pharmacological treatment recommendations and goals have become more aggressive. The dietary modification called the "Dietary Approach to Stop Hypertension" a.k.a the DASH diet has been shown to significantly lower both systolic and diastolic blood pressure. Recent studies suggest that many nutraceuticals have potentially salubrious effects on hypertension. A pilot study was conducted at Logan College using a fruit and vegetable green powder mix drink that purported to provide levels of

phytochemicals similar to the DASH diet. Results on blood pressure reduction displayed similar efficacy as the DASH diet. Considering the compliance hurdles implicit in the DASH diet, it is suggested that clinical investigation in the use of such phytochemical rich fruit and vegetable powders may be a reasonable science-based alternative treatment option for the physician.

HIGH BLOOD PRESSURE: THE SILENT KILLER

Avoid rich foods and gluttony. When you sit to dine with a ruler, note well what is before you, and put a knife to your throat if you are given to gluttony. Do not crave his delicacies, for that food is deceptive. Proverbs 23:1–3

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% of all strokes and heart attacks! The general consensus is to treat hypertension early and endeavor for numbers under 120/80 mm Hg.

These endeavors usually consist of a combination of lifestyle modification and, when indicated, pharmaceutical prescription. As dietary lifestyle changes are difficult, and therefore often lead to poor compliance, and as research over the last decade or two has demonstrated the potential of nutraceuticals to equal the hypotensive benefits of medications, there is much interest in the use of nutraceuticals, alone or in combination, as an alternative approach to the control of hypertension. This chapter will present one such investigation.

Risks, Occurrence, Classification and Treatment Recommendations

Risks and Occurrence

Hypertension is the most common problem for which patients visit physicians. More than one half of all persons older than 65 years have hypertension, which is most usually, isolated systolic hypertension. Improved control of hypertension has contributed to reductions of nearly 60% in stroke-related deaths and 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.

Mild elevations of blood pressure sustained over several decades increases the risk of arteriosclerosis, stroke, myocardial infarction, heart failure, 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 paper is limited to non-complicated, primary pre-hypertension and stage-one hypertension. The goals of therapy are to bring blood pressure (BP) down into the optimal ranges and prevent end-organ damage, especially to the heart, brain, eyes and kidneys.

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*, and is the most common form of uncontrolled hypertension. Isolated systolic blood pressure elevation is recognized as a significant risk factor for vascular complications in patients with hypertension.

Both increased systolic and diastolic blood pressures can increase the risk for target organ diseases (TOD) like congestive heart failure, heart attack, kidney disease, stroke, erectile dysfunction, peripheral vascular disease, and blindness. Nonetheless, some physicians still accept inappropriately high blood pressure measurements, 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 pre-hypertension range (less than 140 mm Hg), even in the presence of normal diastolic blood pressure. Evidence suggests that reduction of the blood pressure by 5 to 6mm Hg can decrease the risk of stroke by 40%, decrease the risk coronary heart disease by 15-20%, and reduce the likelihood of dementia, heart failure, and mortality from vascular disease.

Classification of Blood Pressure: New Consensus Research Data

Hypertension can be mild, moderate, or severe. The National Heart, Lung, and Blood Institute classify blood pressure as normal, pre-hypertension and hypertension stages 1 & 2. *Normal blood pressure* 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 diastolic blood pressure is higher than normal (120/80 mmHg) but not high enough to be considered high blood pressure (140/90 mmHg). Pre-hypertension is therefore a systolic (top number) between 120 and 139 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 159mmHg and a diastolic pressure between 90 and 99 mmHg or higher. *Stage 2 hypertension* is a systolic pressure of 160mmHg or higher, and a diastolic of 100 or higher.

Stages of Hypertension and Treatment Strategies as Recommended by JNC 7

The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) is the latest consensus report from the National High Blood Pressure Education Program of the National Heart, Lung, and Blood Institute. The general change in the guidelines was to treat hypertension sooner!

Pre-hypertension (120 to 139/80 to 89 mm Hg) calls for lifestyle modification (diet, exercise, and weight reduction) with drug therapy reserved for patients with diabetes mellitus or chronic kidney disease. *Stage 1 hypertension* (140 to 159/90 to 99 mm Hg) calls for lifestyle modification and thiazide-type diuretics for most patients. Consideration must be given for other coexisting conditions. *Stage 2 hypertension* (>=160/>=100 mm Hg) calls for lifestyle modification and a two-drug combination for most patients, commonly a diuretic and an ACE inhibitor or beta blocker. Of course, consideration must be given for other coexisting conditions.

When used alone, prescription anti-hypertensive medications average a BP reduction of 12 mm Hg systolic and 6 mm Hg diastolic. Therefore in patients requiring 20/10 reductions two prescriptions are recommended.

Pathophysiology: TOD, ROS, ED and VSM

There is no accepted cause of primary essential hypertension which accounts for 90% of cases of high blood pressure (HBP). The current consensus is that the blood vessel is the primary and central organ in HBP. Of course, there are risk factors that contribute to developing HBP. A number of environmental factors have been implicated in the development of high blood pressure, including, but not limited to, salt intake, obesity, race, physical activity level, heredity, diet, and stress level.

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 from *reactive oxygen species* (ROS) and vascular *smooth muscle dysfunction* (VSM) with its hypertrophy, hyperplasia, and remodeling, may be some of the first events that trigger essential hypertension. Nutrient-gene interactions determine specific phenotypic consequences of vascular health, vascular disease or hypertension.

Endothelial Dysfunction

The vascular endothelium is the largest endocrine organ and the largest organ in the body. It is 14,000 ft^2 in surface area, the size of 6½ 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.

Under normal, healthy physiologic conditions the vascular endothelium forms a continuous sheet of organized monolayer polyhedral cells. However, this becomes disorganized at extremes of hemodynamic shear and stress (hypotension and hypertension).

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, and 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 and Antioxidants

Hypertensive patients have an impaired endogenous and exogenous antioxidant defense mechanism. This includes elevated plasma malondialdehyde (MDA) and hydrogen peroxide (H_2O_2) production by polymorphonuclear neutrophils (PMNs) and NADPH oxidase; reduced superoxide dismutase (SOD) in erythrocytes and polyunsaturated fatty acids (PUFA) on their membranes; normal to low plasma selenium and low reduced glutathione peroxidase (GPX1) and nitric oxide (NO) levels; and low plasma vitamins A, E, and C and copper with increased zinc. In sum, hypertensive patients have more oxidative stress with more reactive oxygen species (ROS) production. This is easily demonstrated by increased lipid peroxidation markers in serum and urine and clinically noted by a greater than normal response to oxidative stress.

Vascular Smooth Muscle Dysfunction

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 nitric oxide (NO). 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.

Of concurrent interest, a small new study by Larsen, 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 Etiology and Nutritional Therapies

Dietary Causes

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, fried foods (potato chips, French fries, fried chicken) and simple carbohydrates can lead not only to high cholesterol levels in the blood, but also to high blood pressure. Such a diet promotes dysglycemia, favors pro-oxidant processes, is low in phytonutrient antioxidants, has a poor Na/K ratio, will be low in magnesium and fiber, and high in pro-inflammatory fats.

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 food groups high in fiber, calcium, potassium, and /or magnesium.

Dietary Approaches to Stop Hypertension (DASH) Diet

A meta-analysis of clinical nutritional and lifestyle changes, reported in the *Journal of Clinical Investigation* in 1993, evaluated the effects of numerous interventions on systolic BP. The most effective intervention was the Dietary Approaches to Stop Hypertension diet, or 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 subsequent 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.

The DASH-I diet published in 1997 was a landmark nutritional trial in reducing blood pressure in hypertensive patients. The DASH-II (low sodium) diet, published in 2001, confirmed the value of DASH-I, but proved that the addition of moderate to severe sodium restriction further enhanced BP reduction.

DASH-I trial design used a selection criteria of Stage-I hypertension (SBP <160, DBP 80-95) with and average age of 45 yrs. There were 379 participants, two-thirds of which were minorities, who followed either the control or treatment diets for 8 weeks. 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.

As compared to the control diet, which mimicked the Standard American Diet (S.A.D.), the DASH diet supplied 3 grams of sodium, with a 6 to 10 Na/K ratio, 10 servings of fruits and vegetables, 31 grams of fiber, and 2.7 servings a day of low fat diary.

Significant reductions in blood pressure were garnered with this controlled feeding of wholegrains, nuts, poultry, fish, low fat diary, and fruits and vegetables, whilst reducing intake of saturated and trans fatty acids, red meat, sweets, sugars and other refined carbohydrates. Specifically, the hypertensive subjects on the DASH diet had BP reductions of 11.4 systolic mm Hg and 5.5 diastolic mm Hg. Minority subjects, especially blacks, had greater reductions in BP compared to white subjects. The reduction in BP occurred almost immediately, and reaching near maximum levels at two weeks, but was sustained throughout the eight-week study. Importantly, the DASH Diet group had reductions in BP that were equal to that obtained with pharmacologic treatment of mild hypertension.

Whole Food Based Concentrates: Fruit, Vegetable, and Fiber Extracts

Studies suggest that 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* formulated from a wide variety 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 on such products. 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 vasodilatation, improved endothelial function, improved arterial compliance, and reductions in both homocysteine and BP.

A DASH of Phytochemicals?

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*."

It had generally been thought that the effectiveness of the DASH diet was largely due to the high fiber, magnesium, potassium, folic acid, and vitamin C content in this fruit and vegetable rich diet. However, recent studies further suggest that it may be that the plethora of phytonutrients in plant foods is responsible for a larger percent of the credit.

Various research reports find that twenty 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. Eleven naturally-occurring substances are noted to have calcium channel blocker activity, eleven have diuretic activity, eleven enhance nitric oxide, sixteen have direct vasodilator properties, and fourteen improve insulin sensitivity. Evidence for benefit is much stronger when multiple foods and nutraceuticals are considered together rather than as isolated components. According to Brent M. Egan, MD Professor of Pharmacology and Medicine at the

Medical University of South Carolina, "*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*."

Over 4,000 naturally occurring *polyphenol 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 anti-hypertensive properties. In addition, they reduce stroke and provide cardio-protective effects that reduce CHD morbidity and mortality.

Lycopene is a non-provitamin-A carotenoid, a 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. Thirty subjects with Stage I hypertension, age 40-65, taking no anti-hypertensive or anti-lipid medications, were 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) with a $p < 0.01$. A similar study of 35 subjects with Stage I hypertension showed similar results on SBP, but not DBP. Of note, serum lipids were significantly improved in both studies without change in serum homocysteine.

Green and black tea contains many active compounds that may alter BP, including flavonoids, which are polyphenolic compounds with vasodilatory and antioxidant effects, these include: theanine, theobromine, quercetin, epigallocatechin-3-0-gallate (EGCG), gamma-glutamylmethylamide (GMA), thearubigins and theaflavins. Still, additional studies in humans will be required to accurately assess these potential BP effects.

Supplement Recommendations

Mark Houston, M.D., summarizes in *JANA* April 2002 those nutritional supplements that have reasonable scientific rationale for their use in hypertension:

Minerals

Potassium.....60 – 100 mEq

Potassium/sodium ratio…….. > 5:1

Magnesium .....500 – 1000 mg

Calcium .....1000 – 1500 mg

Zinc .....25 mg

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

Fats: 25% total calories

A. Omega-3 fatty acids (30%) PUFA .....3 – 4 grams (DHA, EPA, ALA,)

B. Omega-6 fatty acids (10%) PUFA (flax, CLA, canola oil, nuts)

Vitamins

Vitamin C.....250- 500 mg BID

Vitamin E.....400 to 800 IU QD

Vitamin B-6 .....100 mg QD to BID

Misc.

Co-enzyme Q-10 (QGEL®).....60 mg QD to BID

Lipoic Acid .....100 to 200 mg BID

N-Acetyl Cysteine .....500 mg BID

L-Arginine (Heart Bar®) (3.3 grams) 3 gm

Hawthorne Standardized Extract.....160 – 900 mg QD

L-Carnitine.....1000 mg BID

Taurine .....1.0 to 1.5 gm BID

SNADA .....2.5 to 5.0 mg

While these are very thorough recommendations, experience suggests that compliance may be a problem in a significant percentage of patients if lots of pills must be taken multiple times a day. Furthermore, how is the clinician to figure which each patient needs which supplement(s) most?

A FRUIT AND VEGETABLE GREEN POWDER MIX: A SIMPLER, HIGH COMPLIANCE NATURAL ALTERNATIVE?

The Logan Study

The Logan College research, headed by John Zhang, MD, PhD, 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. There was no placebo used with the 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. It was naturally flavored to enhance compliance. The product was formulated with a liposomal nanotechnology to enhance the bioavailability of the lipophillic and poorly water soluble phytonutrients.

One serving of a 12 g scoop mixed in 6-8 ounces of water supplied 50 calories, 1.5 gram (g) fat, 24 mg NA, 152 mg K, 8 g carbohydrates, less than 1 g fiber, 2 g 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 5% 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 2 scoops a day.

Selection criteria were similar to those for the DASH diet study. From the mostly Caucasian student and teacher population were selected candidate with pre-hypertension and Stage I hypertension who were otherwise healthy and taking no medications. Subjects were given 2 scoops a day (total 24 gm) to mix with water (6-12 ounces) to taste. No other lifestyle modifications were made. No adverse events were reported.

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). These findings surpassed both DASH I and II diets and the average pharmaceutical response noted above. No significant blood pressure decrease was observed in the control group.

Discussion

It should be observed that taking the green phytonutrient-rich fruit and vegetable drink for 90 days significantly reduced blood pressure even better than the DASH I and II diets.

This dietary supplement, which provided 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 than the DASH diets, nonetheless exceeded the results of the more restrictive DASH II diet, without concomitant sodium restriction. This study supports the hypothesis that it is indeed the phytochemicals, a.k.a. 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 pre-hypertension and Stage 1 hypertension.

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

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 *vis-à-vis* hypertension.

Considerations

It should be noted that the size of the Logan study was small (20 active subjects, 20 control). Further testing on a larger base is warranted to confirm results. A critical analysis of the

Logan study also notes that there were no placebos used with the controls. As of this writing, two college and university follow up studies are being conducted, using placebo controls.

Although antioxidant and macro and micro nutrient data were provided on the green fruit and vegetable phytonutrient powder, no measure of nitrates were taken making it impossible to determine to what extent the nitrate content may be responsible for the results. Such measurements are being conducted as of this writing.

There is also the effect of stevia. Natural Standard Monographs rank stevia, along with Co Q10, as having a Grade B rating (A, B, C, D, F scale) for scientific proof as relates to lowering blood pressure. Therapeutic adult dosing for stevia is 250-500 mg / day, TID. The green phytonutrient, which used stevia to enhance compliance, supplied 400 mg stevia per day.

As to the use of phytonutrient supplements in general, 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 practitioner. The terms “all natural”, “organic”, “herbal”, etc., do not necessarily imply potency, purity, safety, or efficacy.

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 on going

SUMMARY AND CONCLUSIONS

Vascular biology (ED and VSM dysfunction) plays a primary role in the initiation and perpetuation of the “Silent Killer”, hypertension and its sequela of CVD and TOD. 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.

Whole food and whole food concentrates of fruits, vegetables and fiber with natural combinations of balanced 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. Nonetheless, in the treatment of hypertension there is likely a role for the selected use of both single and component nutraceuticals, vitamins, antioxidants, and minerals, based on scientifically controlled studies, as a complement to optimal nutritional dietary intake from food along with other lifestyle modifications.

Optimal nutrition, nutraceutical supplements, vitamins, antioxidants, minerals, weight loss, exercise, smoking cessation, and judicious restriction of alcohol and caffeine, as well as other lifestyle modifications, can prevent, delay the onset, reduce the severity, treat, and control the essential hypertension of many patients. An integrative and synergistic approach combining these lifestyle modifications with appropriate pharmacologic treatment is most likely to achieve new goal blood pressure levels, reduce risk factors for vascular disease, improve vascular biology and vascular health, optimize target organ protection, and reduce coronary heart disease, stroke, congestive heart failure, and renal disease. It may be that the use of pharmaceutical grade green fruit and vegetable concentrates that provide the phytonutrients of ten servings of fruits and vegetables can be considered as a rational natural alternative that can yield results similar to the DASH diet when compliance to said diet proves too difficult.

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