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The role of cellular micronutrient analysis, nutraceuticals, vitamins, antioxidants and minerals in the prevention and treatment of hypertension and cardiovascular disease

Mark C. Houston

Abstract: Macronutrient and micronutrient deficiencies are very common in the general population and may be even more common in patients with hypertension and cardiovascular disease due to genetic, environmental causes and prescription drug use. The Hypertension Institute in Nashville, TN, has evaluated micronutrient deficiencies and oxidation status, in a group of hypertensive versus normotensive patients. There are significant differences in numerous intracellular micronutrients and oxidation status between these two groups. Replacement of the micronutrient deficiencies, as well as high-dose therapy of selected nutraceuticals in combination with optimal diet, exercise and weight management resulted in control of blood pressure to goal levels in 62% of the hypertensive population (as defined by JNC 7) over a period of 6 months with complete tapering and discontinuation of antihypertensive drugs. These deficiencies will have an enormous impact on present and future cardiovascular health and outcomes such as hypertension, myocardial infarction, stroke and renal disease and overall health costs. It is estimated that the annual savings in drug costs alone for the treatment of hypertension could be as much as US$10 billion. Diagnosis and treatment of these nutrient deficiencies and improvement in oxidation status using functional intracellular assessments will reduce blood pressure, improve vascular health, endothelial dysfunction, vascular biology and cardiovascular events. Vascular biology assumes a pivotal role in the initiation and perpetuation of hypertension and target organ damage sequelae. Endothelial activation, oxidative stress, inflammation and vascular smooth muscle dysfunction are initial events that start hypertension. Nutrient–gene interactions determine a broad array of phenotypic consequences such as vascular problems and hypertension. Optimal nutrition, nutraceuticals, vitamins, antioxidants, minerals, weight loss, exercise, smoking cessation and moderate restriction of alcohol and caffeine in addition to other lifestyle modifications can prevent and control hypertension in many patients. An integrative approach combining these lifestyle suggestions with the correct pharmacologic treatment will best achieve new goal blood pressure levels, reduce cardiovascular risk factors, improve vascular biology and vascular health, reduce cardiovascular target organ damage and reduce healthcare expenditure. The expanded scientific roles for nutraceutical supplements are discussed in relation to the prevention and treatment of essential hypertension and cardiovascular diseases with emphasis on mechanisms of action and clinical integration with drug therapy with hypertension guidelines. It is the purpose of this paper to review only the hypertension clinical trials that have evaluated the clinical use and efficacy of nutrition, weight loss, exercise and selected nutritional supplements, vitamins, minerals and antioxidants. Numerous clinical trials have evaluated the use of nutritional supplements such as beta carotene, selenium, vitamin C and vitamin E in the prevention of coronary heart disease and stroke yielding conflicting results (positive, neutral and negative). In many of these clinical trials there are enormous clinical design problems, methodologic flaws, varied patient population, variable dose and type of
vitamin use, improper selection of vitamin used and many other issues that make the studies difficult to interpret. It is beyond the scope of this paper to review these trials. The reader is referred to the vast literature on this subject.

**Keywords:** functional intracellular assessments, hypertension, natural treatment, nutrition, antioxidants and hypertension

**Introduction**

Hypertension is a consequence of the interaction of genetics and the environment. Macronutrients and micronutrients are crucial in the regulation of blood pressure (BP) and subsequent target organ damage (TOD). Nutrient–gene interactions, subsequent gene expression, oxidative stress and inflammation have positive or negative influences on vascular biology in humans. Endothelial dysfunction (ED) and vascular smooth muscle dysfunction (VSMD) initiate and perpetuate essential hypertension. The optimal combination of macronutrients and micronutrients has a significant impact on the prevention, treatment and the potential vascular complications of hypertension [Houston, 2007]. Optimal medical practice using functional intracellular assessments is recommended to diagnose and treat macronutrient and micronutrient deficiencies in order to effectively treat hypertension and related cardiovascular events.

The transition from the Paleolithic diet to our modern diet has produced an epidemic of nutritionally related diseases including hypertension, atherosclerosis, coronary heart disease (CHD), myocardial infarction (MI), congestive heart failure (CHF), cerebrovascular accidents (CVA), renal insufficiency (RI), renal failure (RF), type 2 diabetes mellitus (DM), metabolic syndrome and obesity [Houston, 2007; Eaton et al. 1997]. Short-term reduction in BP utilizing nutrition results in intermediate and long-term improvements in morbidity and mortality, including CVA, CHD and MI [Houston, 2007; Eaton et al. 1997].

**Nutrition and disease prevention**

An integrative approach that uses nutrition, vitamins, antioxidants, minerals, functional foods, nutraceuticals, weight loss, exercise, judicious use of alcohol and caffeine with tobacco cessation combined with optimal pharmacologic therapy is the best means to reduce BP and TOD in most hypertensive patients. Proper diagnosis of nutrient deficiencies using functional intracellular assessment is recommended in order to initiate the best nutrient replacement therapy. To achieve lower BP goals will require a combination of lifestyle modifications and drug therapy [Houston, 2007; The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, 2003; Eaton et al. 1997].

Such lifestyle changes may prevent or delay the onset of hypertension, reduce BP levels and the progression of cardiovascular disease (CVD) and allow for fewer drugs and/or lower doses. Finally, there may be additive or synergistic improvements in cardiovascular risk factors, vascular function, structure and health [Houston, 1992, 2007]. About 50–60% of essential hypertensive patients are excellent and appropriate candidates for preliminary and prolonged lifestyle modifications as long as the BP is evaluated frequently and clinical TOD, CCD, DM or significant risk factors are not present at that time and do not develop later [The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, 2003; Houston, 1994]. In this paper we review the basic science and clinical studies of functional intracellular assessment, nutraceutical supplements, vitamins, antioxidants, minerals, macronutrients and micronutrients and their impact on the prevention and treatment of hypertension. It is important to integrate nutrition and nutraceutical science with traditional drug therapy to reduce BP, TOD and improve the dismal statistics of BP control worldwide [Houston, 2007; Wolf-Maier et al. 2003].

**Hypertension and oxidative stress in humans**

Oxidative stress with an imbalance between reactive oxygen species (ROS) and the antioxidant defense mechanisms may contribute to the etiology of hypertension in animals [Nayak et al. 2001]
and humans [Kitiyakara and Wilcox, 1998]. Hypertensive patients have an impaired endogenous and exogenous antioxidant defense mechanism [Russo et al. 1998]. In addition, hypertensive patients have more oxidative stress with more ROS produced and a greater-than-normal response to oxidative stress [Russo et al. 1998; Tse et al. 1994].

The proposed mechanisms of ROS-induced hypertension in humans is shown in Box 1. Antioxidant deficiency and excess free-radical production have been implicated in human hypertension in numerous epidemiologic, observational and interventional studies [Russo et al. 1998; Galley et al. 1997; Tse et al. 1994].

A summary of the present research and conclusions of the role of oxidative stress in animal and human hypertension is shown in Box 2. The interrelations of neurohormonal systems, oxidative stress and cardiovascular disease is shown in Figure 1. The increased oxidative stress and inflammation in human hypertension is thus a combination of increased generation of ROS, an exacerbated response to ROS and a decreased antioxidant reserve [Saez et al. 2001; Dhalla et al. 2000; Russo et al. 1998; Galley et al. 1997; Tse et al. 1994].

**Evolutionary nutrition**

Humans have evolved from a preagricultural, hunter-gatherer society to a commercial agriculture with highly processed, refrigerated and fast foods that have imposed an unnatural and unhealthy nutrition. The human genetic makeup is 99.9% that of our Paleolithic ancestors, yet our nutritional, vitamin and mineral intakes are vastly different [Eaton et al. 1997]. The macronutrient and micronutrient variations contribute to the higher incidence of hypertension and other CVDs through a complex nutrient–gene interaction (Figure 2) [Talmud and Waterworth, 2000; Berdanier, 1996]. Poor nutrition, coupled with obesity and a sedentary lifestyle have resulted in an exponential increase in nutritionally related diseases. In particular, the high Na+/K+ ratio of modern diets has contributed to hypertension, stroke, CHD, CHF and renal disease [Eaton et al. 1997]. In addition, the relatively low intake of omega-3 polyunsaturated fatty acids (PUFA), increase in omega-6 PUFA saturated fat and trans fatty acids, has contributed to the increased incidence of CHD, hypertension, DM and hyperlipidemia [Broadhurst, 1997].

**Sodium (Na+)**

The average sodium intake in the US is 5000 mg per day with some areas of the country consuming 15,000–20,000 mg per day [Kotchen and McCarron, 1998]. However, the minimal requirement for sodium is probably about 500 mg per day [Kotchen and McCarron, 1998]. Epidemiologic, observational and controlled clinical trials demonstrate that an increased sodium intake is associated with higher BP [Kotchen and McCarron, 1998]. A reduction in sodium intake in hypertensive patients, especially the salt-sensitive patients, will significantly lower BP by 4–6/2–3 mmHg that is proportional to the severity of sodium restriction [Svetkey et al. 1999; Cutler et al. 1997].

Sodium does have a major impact on cardiovascular, cerebrovascular and renal disease [Messerli et al. 1997; Kawasaki et al. 1978]. Studies have documented a direct relationship between...
sodium intake and increased platelet reactivity, stroke (independent of BP), left ventricular hypertrophy, MI, CHF sudden death and left ventricular filling [Messerli et al. 1997; Kawasaki et al. 1978]. The renal plasma flow falls and glomerular filtration rate and glomerular filtration increase leading to an increase in intraglomerular capillary pressure, microalbuminuria,
proteinuria, glomerular injury and renal insufficiency. Sodium also reduces arterial compliance, independently of BP changes [Messerli et al. 1997; Kawasaki et al. 1978].

Salt sensitivity (>10% increase in mean arterial pressure [MAP] with salt loading) is a key factor in determining the cardiovascular, cerebrovascular, renal and BP response to dietary salt intake [Weinberger, 1996]. Cardiovascular events are more common in the salt-sensitive patients than in salt-resistant ones, independent of BP [Morimoto et al. 1997].

The evidence is very suggestive that a reduction in dietary salt intake reduces TOD (brain, heart, kidney and vascular) that is both dependent on the small BP reduction, but also independent of the decreased BP [Messerli et al. 1997; Kawasaki et al. 1978]. A balance of sodium with other nutrients is important, not only in reducing and controlling BP, but also in decreasing cardiovascular and cerebrovascular events.

**Potassium (K+)**
The average US dietary intake of potassium (K+) is 45 mEq per day with a potassium to sodium (K+/Na+) ratio of less than 1:2 [Houston and Harper, 2008]. The recommended intake of K+ is 650 mEq per day with a K+/Na+ ratio of over 5:1. Numerous epidemiologic, observational and clinical trials have demonstrated a significant reduction in BP with increased dietary K+ intake [Houston and Harper, 2008; Whelton and He, 1999]. The magnitude of BP reduction with a K+ supplementation of 60–120 mEq per day is 4.4/2.5 mmHg in hypertensive patients. Alteration of the K+/Na+ ratio to a higher level is important for antihypertensive as well as cardiovascular and cerebrovascular effects [Gu et al. 2001]. High potassium intake reduces the incidence of cardiovascular and cerebrovascular accidents independent of the BP reduction [Houston and Harper, 2008; Gu et al. 2001; Whelton and He, 1999]. Gu et al. demonstrated for the first time that potassium supplementation at 60 mmol of KCl per day for 12 weeks significantly reduced systolic BP by 5.0 mmHg (range 2.13 mmHg to 7.88 mmHg; p < 0.001) in 150 Chinese men and women aged 35–64 years.

**Magnesium (Mg++)**
A high dietary intake of magnesium of at least 500–1000 mg per day reduces BP in most of the reported epidemiologic, observational and clinical trials, but the results are less consistent than those seen with Na+ and K+ [Houston and Harper, 2008; Widman et al. 1993]. In most epidemiologic studies, there is an inverse relationship between dietary magnesium intake and BP [Laurant and Touyz, 2000]. A study of 60 essential hypertensive subjects given magnesium supplements showed a significant reduction in BP over an 8-week period documented by 24-hour ambulatory BP, home and office BP.

Magnesium competes with Na+ for binding sites on vascular smooth muscle and acts like a calcium channel blocker, increases PGE, binds in a necessary-cooperative manner with potassium, inducing vasodilation and BP reduction.

Magnesium is an essential cofactor for the delta-6-desaturase enzyme that is the rate-limiting step for conversion of linoleic acid to gamma-linolenic acid (GLA). GLA elongates to form dihomo-gamma-linolenic acid (DGLA), the precursor of prostaglandin E1, a vasodilator and platelet inhibitor. Magnesium regulates systolic and diastolic BP, intracellular Ca++, Na+, K+ and pH as well as left ventricular mass, insulin sensitivity and arterial compliance.

**Calcium (Ca++)**
Population studies show a link between hypertension and calcium [McCarron, 1997], but clinical trials that administer calcium supplements to patients have shown inconsistent effects on BP [Houston and Harper, 2008; McCarron, 1997]. The heterogeneous responses to calcium supplementation have been explained by Resnick [1991]. This is the ‘ionic hypothesis’ of hypertension, cardiovascular disease and associated metabolic, functional and structural disorders.

**Zinc (Zn++)**
Low serum zinc levels in observational studies correlate with hypertension as well as CHD, type II DM, hyperlipidemia, elevated lipoprotein a, 2-hour postprandial plasma insulin levels and insulin resistance [Garcia Zozaya and Padilla Viloria, 1997]. Bergomi et al. [1997] evaluated Zn++ status in 60 hypertensive compared with 60 normotensive control subjects. An inverse correlation of BP and serum Zn++ was observed. The BP was also inversely correlated to a Zn++-dependent enzyme-lysyl oxidase activity. Zn++ inhibits gene expression and transcription through nuclear
factor kappa-B and activated protein-1. These effects plus those on insulin resistance, membrane ion exchange, renin—angiotensin system (RAAS) and SNS effects may account for Zn\(^{++}\) antihypertensive effects. Zinc intake should be between 15–30 mg per day [Houston, 2007].

**Protein**
Observational and epidemiologic studies demonstrate a consistent association between a high protein intake and a reduction in BP [Stamler et al. 1996]. The protein source is an important factor in the BP effect, animal protein being less effective than nonanimal protein [Elliott et al. 2000; Stamler et al. 1996]. However, lean or wild animal protein with less saturated fat and more essential omega-3 and omega-6 fatty acids may reduce BP, lipids and CHD risk.

Fermented milk supplemented with whey protein concentrate significantly reduced BP in human studies [Pins and Keenan, 2006; Aihara et al. 2005; Fitzgerald et al. 2004]. Administration of 20 g per day of hydrolyzed whey protein supplement rich in bioactive peptides significantly reduced BP over 6 weeks by 8.0 ± 3.2 mmHg in systolic BP and 5.5 ± 2.1 mmHg in diastolic BP [Pins and Keenan, 2006]. Powdered fermented milk with *Lactobacillus helveticus*, which contains two inhibitory peptides for angiotensin-converting enzyme (ACE), significantly lowered BP by 11.2/6.5 mmHg in 4 weeks.

Pins and Keenan [2006] administered 20 g of hydrolyzed whey protein to 30 hypertensive subjects and noted a BP reduction of 11/7 mmHg compared with controls at 1 week that was sustained throughout the study. These data indicate that the whey protein must be hydrolyzed in order to exhibit an antihypertensive effect, and the maximum BP response is dose dependent.


Sardine muscle protein, which contains Valyl-Tyrosine (VAL-TYR), significantly lowers BP in hypertensive subjects [Kawasaki et al. 2000]. Kawasaki *et al.* treated 29 hypertensive subjects with 3 mg of VAL-TYR sardine muscle concentrated extract for 4 weeks and lowered BP by 9.7/5.3 mmHg (*p* < 0.05). Levels of A-I increased as serum A-II and aldosterone decreased indicating that VAL-TYR is a natural ACEI. A similar study with a vegetable drink with sardine protein hydrolysates significantly lowered BP by 8/5 mmHg in 13 weeks [Kawasaki *et al.* 2002].

In addition to ACEI effects, protein intake may also alter catecholamine responses and induce natriuresis. Low protein intake coupled with low omega-3 fatty acid intake may contribute to hypertension in animal models [Begg *et al.* 2009]. The optimal protein intake, depending on level of activity, renal function, stress and other factors, is about 1.0 to 1.5 g/kg/day [Houston, 2008].

**Fats**
Observational, epidemiologic, biochemical, cross-sectional studies and clinical trials of the effect of fats on BP have been disappointing and inconsistent [Morris, 1994].

**Omega-3 PUFA**
Alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexanoic acid (DHA) comprise the primary members of the omega-3 PUFA family. Omega-3 fatty acids are found in coldwater fish (herring, haddock, Atlantic salmon, trout, tuna, cod and mackerel), fish oils, flax, flax seed, flax oil and nuts [Mori *et al.* 1999, 2009; Ueshima *et al.* 2007]. It has been suggested that an increase in omega-3 fatty acid intake can lower BP by 5/3 mmHg [Bønaa *et al.* 1999, 2004]. Administration of fish oils, flax, flax seed, flax oil and nuts [Mori *et al.* 1999; Bønaa *et al.* 1999, 2009; Ueshima *et al.* 2007; Mon, 2006; Bønaa *et al.* 1990]. The studies on the effects of fish oil on BP have shown a dose-related response in hypertension as well as a relationship to the specific concomitant diseases associated with hypertension.

Studies indicate that DHA is very effective in reducing BP and heart rate [Mori *et al.* 1999]. However, formation of EPA and ultimately DHA from ALA is decreased in the presence of increased linoleic acid in the diet (omega-6 fatty acid), increased dietary saturated fats and trans fatty acids, alcohol and aging through inhibitory effects or reduced activity of delta-6-desaturase, delta-5-desaturase or delta-4-desaturase. Eating coldwater fish three times per week is as effective as high-dose fish oil in reducing BP in
hypertensive patients, and the protein in the fish may also have antihypertensive effects.

The omega-6 fatty acid family, which includes linoleic acid (LA), GLA, DGLA and arachidonic acid (AA) do not usually lower BP significantly, but may prevent increases in BP induced by saturated fats [Morris, 1994]. The ideal ratio of omega-3 fatty acid to omega-6 fatty acid is between 1:1 to 1:2 with a polyunsaturated to saturated (P/S) fat ratio greater than 1.5 to 2:0 [Eaton et al. 1997].

The omega-3 FA have a multitude of other cardiovascular consequences whose interplay modulates BP [Chin, 1994].

**Omega-9 fatty acids**

Olive oil is rich in monounsaturated fats (MUFA: omega-9 fatty acid, oleic acid), which have been associated with BP and lipid reduction in Mediterranean and other diets [Ferrara et al. 2000; Thomsen et al. 1995]. In one study, the systolic BP fell 8 mmHg ($p < 0.05$) and the diastolic BP fell 6 mmHg ($p < 0.01$) in the MUFA-treated subjects compared with the PUFA-treated subjects [Ferrara et al. 2000]. In addition, the need for antihypertensive medications was reduced by 48% in the MUFA group versus 4% in the PUFA (omega-6 FA) group ($p < 0.005$).

Olive oil is rich in oleic acid (omega-9 FA). Extra virgin oil has 5 mg of phenols in 10 g of olive oil, a rich polyphenol antioxidant. About four tablespoons of extra virgin olive oil is equal to 40 g. Other fats such as palmitoleic acid may decrease BP and reduce CVA from intracranial hemorrhage [Houston, 2007].

**Fiber**

The clinical trials with various types of fiber to reduce BP have been inconsistent [He and Whelton, 1999]. Soluble fiber, guar gum, guava, psyllium and oat bran reduce BP and reduce the need for antihypertensive medications in hypertensive subjects, diabetic subjects and hypertensive–diabetic subjects.

**Garlic**

Good clinical trials utilizing the correct type, long acting preparations and dose of garlic have shown consistent reductions in BP in hypertensive patients with an average reduction in BP of 8.4/7.3 mmHg [Simons et al. 2009; Reinhard et al. 2008].

Not all garlic preparations are processed similarly and are not comparable in antihypertensive potency [Houston, 2007]. In addition, cultivated garlic (*Allium sativum*), wild uncultivated garlic or bear garlic (*Allium ursinum*) and aged or fresh garlic and long-acting garlic preparations will have variable effects [Simons et al. 2009; Reinhard et al. 2008].

Approximately 10,000 µg of allicin (one of the active ingredients in garlic) per day, the amount contained in four cloves of garlic (4 g) is required to achieve a significant BP-lowering effect [Houston, 2007]. In humans the average reduction in systolic BP is 5–8 mmHg.

**Tea: green and black**

The effects of chronic green or black tea ingestion on BP in humans has not been studied extensively and results are inconsistent [Hodgson et al. 1999]. However, green tea, black tea and extracts of active components in both teas have demonstrated reduction in BP.

**Seaweed**

Wakame (*Undaria pinnatifida*) is the most popular edible seaweed in Japan [Suetsuna and Nakano, 2000]. In humans, 3.3 g daily of dried Wakame for 4 weeks significantly reduced both the systolic BP 14 + 3 mmHg and the diastolic BP 5 + 2 mmHg ($p < 0.01$) [Nakano et al. 1998]. In a study of 62 middle-aged, male subjects with mild hypertension given a potassium-loaded, ion-exchanging sodium-adsorbing potassium-releasing seaweed preparation showed significant BP reductions at 4 weeks on 12 and 24 g/day of the seaweed ($p < 0.01$) [Krotkiewski et al. 1991]. The mean arterial pressure fell 11.2 mmHg ($p < 0.001$) in the sodium-sensitive subjects and 5.7 mmHg ($p < 0.05$) in the sodium-insensitive subjects, which correlated with plasma renin activity.

Seaweed and sea vegetables contain almost all of the seawater’s 77I minerals and rare earth elements, fiber and alginate in a colloidal form [Suetsuna and Nakano, 2000]. The primary effect of Wakame appears to be through its ACEI activity from at least four parent tetrapeptides and possibly their dipeptide and tripeptide metabolites, especially those containing the amino acid sequence TYR-LYS in some
combination [Suetsuna and Nakano, 2000]. Its long-term use in Japan has demonstrated its safety. Other varieties of seaweed may reduce BP by reducing intestinal sodium absorption and increasing intestinal potassium absorption [Krotkiewski et al. 1991].

**Natural ACEIs**

Many other foods have demonstrated ACEI activity *in vitro*, but whether they are active after oral ingestion *in vivo* remains to be proven in human studies [Houston, 2007].

**Vitamin C**

Vitamin C is a potent water-soluble antioxidant that recycles vitamin E, improves ED and produces a diuresis [Sherman et al. 2000]. Numerous epidemiologic, observational and clinical studies have demonstrated that the dietary intake of vitamin C or plasma ascorbate concentration in humans is inversely correlated to systolic and diastolic BP and heart rate [Sherman et al. 2000; Duffy et al. 1999; Ness et al. 1996]. Long-term epidemiologic and observational follow-up studies in humans also show a reduced risk of CVD, CHD and CVA with increased vitamin C intake [Enstrom et al. 1992].

Evaluation of published clinical trials indicate that 250 mg twice daily will lower BP about 7/4 mmHg, improve arterial compliance, improve endothelial function, reduce serum aldehydes, enhance the efficacy of amlodipine, decrease the binding affinity of the AT 1 receptor for angiotensin II and enhance antihypertensive effects of medications in the elderly with refractory hypertension [Ledlerc et al. 2009; Block et al. 2008; Hatzitolios et al. 2008; Mahajan et al. 2007; Plantinga et al. 2007; Sato et al. 2006]. The lower the initial ascorbate serum level the better is the BP response. The systolic BP and 24 ABM show the most significant reductions with Vitamin C administration orally over time. Block et al. [2001] in an elegant depletion–repletion study of vitamin C demonstrated an inverse correlation of plasma ascorbate levels and systolic and diastolic BP. The multitude of proposed mechanisms for vitamin C in hypertension and other CVDs is outlined in Box 3 [Houston, 2007].

Combined nutrients, vitamins, minerals and antioxidants have clearly been shown to lower BP. Although these varied diets confer more antihypertensive and cardiovascular benefits than any single nutrient, it is also quite probable that vitamin C as a single nutrient plays a significant role in the regulation of BP in normotensive and hypertensive patients. Almost all studies and reviews reported have shown an inverse relationship to vitamin C intake and plasma ascorbate levels that is reasonably consistent among different study groups, populations and the variable study designs. Hypertensive subjects were found to have significantly lower plasma ascorbate levels compared with normotensive subjects (40 versus 57 μmol/liter, respectively) [National Center for Health Statistics, 1982]. Evidence supports the fact that plasma ascorbate is inversely correlated with BP even in healthy, normotensive individuals [Block et al. 2001]. The NHANES-II Study found 20% of US males have plasma ascorbate levels below 27 μmol/liter and 30% of US Black males were below 27 μmol/liter [National Center for Health Statistics, 1982]. This increased prevalence of lower plasma ascorbate levels in Black males could partially account for the higher prevalence of hypertension in Black Americans.

**Vitamin E**

The relationship of vitamin E and BP has been studied in humans [Ward et al. 2007]. Patients with type 2 DM and hypertension on prescription medications with an average BP of 136/76 mmHg were administered mixed tocopherols. The BP actually increased by 7/5.3 mmHg in the study patients. This may be a reflection of drug interactions with tocopherols via Cytochrome P 450 and reduction in the serum levels of the pharmacologic treatments that were

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**Box 3. Proposed mechanisms of vitamin C in hypertension.**

- Reduces ED and improves EDVD, lowers BP and SVR
- Diuresis
- Increases NO and PGI2
- Decreases adrenal steroid production
- Improves sympathovagal balance
- Decreases cytosolic Ca++
- Antioxidant
- Recycles vitamin E, glutathione and uric acid
- Decreases neuroendocrine peptides
- Reduces thrombosis and decreases TxA2
- Decreases lipids (TC, LDL, TG) and raises HDL
- Reduces leukotrienes
- Improves aortic collagen, elasticity and aortic compliance
- Increases cGMP and activates VSM K+ channels
simultaneously being given [Ward et al. 2007]. If vitamin E has an antihypertensive effect, it is probably small and may be limited to untreated hypertensive patients or those with known vascular disease or other concomitant problems such as diabetes or hyperlipidemia.

**Vitamin D**

Epidemiological, clinical and experimental investigations all demonstrate a relationship between the plasma levels of 1,25 (OH)2 D3 (1,25-dihydroxycholecalciferol), the active form of vitamin D and BP [Bednarski et al. 2007; Li et al. 2002; Pfeifer et al. 2001; Hanni et al. 1995], including a vitamin-D-mediated reduction in BP in hypertensive patients. Vitamin D may have an independent and direct role in the regulation of BP and insulin metabolism. Vitamin D3 influences BP by its effects on calcium-phosphate metabolism, RAAS, immune system, control of endocrine glands and ED. Vitamin D3 markedly suppresses renin transcription by a Vitamin D receptor (VDR)-mediated mechanism in cell cultures. Its role in electrolytes, volume and BP homeostasis indicates that Vitamin D3 is important in amelioration of hypertension.

The hypotensive effect of vitamin D was inversely related to the pretreatment serum levels of 1,25 (OH)2 D3 and additive to antihypertensive medications. Pfeifer et al. [2001] showed that short-term supplementation with vitamin D3 and calcium is more effective in reducing systolic BP than calcium alone. In a group of 148 women with low 25 (OH)2 D3 levels, the administration of 1200 mg calcium plus 800 IU of vitamin D3 reduced systolic BP by 9.3% (p < 0.02) compared with 1200 mg of calcium alone. The heart rate fell 5.4% (p = 0.02), but diastolic BP was not changed.

**Vitamin B6 (Pyridoxine)**

Low serum vitamin B6 levels are associated with hypertension in humans [Keniston and Enriquez, 1990]. One human study by Aybak et al. [1995] proved that high-dose vitamin B6 significantly lowered BP. This study compared nine normotensive men and women with 20 hypertensive subjects, all of whom had significantly higher BP, plasma NE and heart rate compared with control normotensive subjects. Subjects received 5 mg/kg/day of vitamin B6 for 4 weeks. The systolic BP fell from 167 ± 13 mmHg to 153 ± 15 mmHg, an 8.4% reduction (p < 0.01) and the diastolic BP fell from 108 ± 8.2 mmHg to 98 ± 8.8 mmHg, a 9.3% reduction (p < 0.005).

**Flavonoids**

Over 4000 naturally occurring flavonoids have been identified in such diverse substances as fruits, vegetables, red wine, tea, soy and licorice [Moline et al. 2000]. 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 cardioprotective effects that reduce CHD morbidity and mortality [Knekt et al. 1994].

Resveratrol is a potent antioxidant and antihypertensive found in the skin of red grapes and in red wine. Resveratrol administration to humans reduces augmentation index, improves arterial compliance and lowers central arterial pressure [Karatzi et al. 2005]. Human subjects were administered 250 ml of either regular or dealcoholized red wine. There was a significant reduction in the aortic augmentation index of 6.1% with the dealcoholized red wine and 10.5% with regular red wine. The central arterial pressure was significantly reduced by dealcoholized red wine at 7.4 mmHg and 5.4 mmHg by regular red wine.

**Lycopene (carotenoid)**

Lycopene is a nonprovitamin-A carotenoid, potent antioxidant found in tomatoes and tomato products, guava, pink grapefruit, watermelon, apricots and papaya in high concentrations [Paran et al. 2009; Reid et al. 2009; Engelhard et al. 2006; Paran and Engelhard, 2001a, 2001b]. Lycopene has recently been shown to produce a significant reduction in BP, serum lipids and oxidative stress markers. Paran and Engelhard [2001b] evaluated 30 subjects with Grade I hypertension, age 40–65, taking no antihypertensive or antilipid medications treated with a tomato lycopene extract for 8 weeks. The systolic BP was reduced from 144–135 mmHg (9 mmHg reduction, p < 0.01) and diastolic BP fell from 91 to 84 mmHg (7 mmHg reduction, p < 0.01). A similar study of 35 subjects with Grade I hypertension showed similar results on systolic BP, but not diastolic BP [Paran and Engelhard, 2001a]. Engelhard gave a tomato extract to 31 hypertensive subjects over 12 weeks demonstrating a significant BP reduction of 10/4 mmHg. Patients on
Various antihypertensive agents had a significant BP reduction of 5.4/3 mmHg over 6 weeks when administered a standardized tomato extract [Paran et al. 2009]. Other studies have not shown changes in BP with lycopene [Reid et al. 2009].

**Coenzyme Q-10 (ubiquinone)**

Coenzyme Q-10 (Co-Q-10) is a potent lipid phase antioxidant, free radical scavenger, cofactor and coenzyme in mitochondrial energy production and oxidative phosphorylation that lowers systemic vascular resistance (SVR), lowers BP and protects the myocardium from ischemic reperfusion injury [Houston, 2007; Burke et al. 2001; Langsjoen and Langsjoen, 1999; Singh et al. 1999a, 1999b]. Co-Q-10 improves mitochondrial energy production, enhancing myocardial infusion with improved diastolic function, left ventricle function, left ventricle wall tension and New York Heart Association class for chronic heart failure.

Serum levels of Co-Q-10 decrease with age and are lower in patients with diseases characterized by oxidative stress such as hypertension, chronic heart disease, hyperlipidemia, DM, atherosclerosis and in those who are involved in aerobic training, patients on total parenteral nutrition, those with hyperthyroidism and patients who take statin drugs [Houston, 2007]. Enzymatic assays showed a deficiency of Co-Q-10 in 39% of 59 patients with essential hypertension versus only 6% deficiency in controls ($p < 0.01$). There is a high correlation of Co-Q-10 deficiency and hypertension in hypertensive subjects following oral administration of 100–225 mg per day of Co-Q-10 [Houston, 2007; Burke et al. 2001; Langsjoen and Langsjoen, 1999; Singh et al. 1999a, 1999b]. Co-Q-10 improves mitochondrial energy production, enhancing myocardial infusion with improved diastolic function, left ventricle function, left ventricle wall tension and New York Heart Association class for chronic heart failure.

In summary, Co-Q-10 has consistent and significant antihypertensive effects in patients with essential hypertension. The major conclusions from in-vitro, animal and human clinical trials indicate the following:

- Compared with normotensive patients, essential hypertensive patients have a high incidence of Co-Q-10 deficiency documented by serum levels.
- Doses of 120–225 mg per day of Co-Q-10, depending on the delivery method and

Concomitant ingestion with a fatty meal, are necessary to achieve a therapeutic level of over 2 μg/ml. This dose is usually 1–2 mg/kg/day of Co-Q-10. Use of a special delivery system allows better absorption and lower oral doses.

- Patients with the lowest Co-Q-10 serum levels may have the best antihypertensive response to supplementation.
- The average reduction in BP is about 15/10 mmHg based on reported studies.
- The antihypertensive effect takes time to reach its peak level, usually at about 4 weeks, then BP remains stable. The antihypertensive effect is gone within 2 weeks after discontinuation of Co-Q-10.
- Approximately 50% of patients on antihypertensive drugs may be able to stop between one and three agents. Both total dose and frequency of administration may be reduced.
- Even high doses of Co-Q-10 have no acute or chronic adverse effects.

Other favorable effects on cardiovascular risk factors include improvement in the serum lipid profile and carbohydrate metabolism with reduced glucose and improved insulin sensitivity, reduced oxidative stress, reduced heart rate, improved myocardial LV function and oxygen delivery and decreased catecholamine levels.

**Alpha-lipoic acid**

Alpha-lipoic acid is a potent and unique thiol compound-antioxidant that is soluble in water and lipids [Houston, 2007]. Alpha-lipoic acid helps to recirculate tissue and blood levels of vitamins and antioxidants in both lipid and water compartments such as vitamin C and E, glutathione and cysteine. Most studies are in the SHR regarding the effects of alpha-lipoic acid on the vasculature and BP, with only one human study [McMackin et al. 2007].

The only human study published to date evaluated alpha-lipoic acid and acetyl-l-carnitine in combination in 36 patients with CHD and hypertension, with or without metabolic syndrome. The brachial artery diameter increased by 2.3% ($p = 0.008$). BP was decreased in the overall group but significantly in those with BP above the median (151 ± 20 to 142 ± 18 mmHg; $p = 0.03$) and in the subgroup with metabolic syndrome (139 ± 21 to 130 ± 18 mmHg; $p = 0.03$) [McMackin et al. 2007].
L-arginine
L-arginine is the primary precursor for the production of nitric oxide (NO), which has numerous cardiovascular effects, mediated through conversion of L-arginine to NO by eNOS to increase cyclic GMP levels in vascular smooth muscle, improve ED and reduce vascular tone and BP [Houston, 2007; Siani et al. 2000]. Patients with hypertension, hyperlipidemia and atherosclerosis have elevated serum levels of asymmetric dimethylarginine, which activates NO [Vallance et al. 1992].

Human studies in hypertensive and normotensive subjects of parenteral and oral administrations of L-arginine demonstrate an antihypertensive effect. The BP decreased significantly on 10 g per day by 6.2/6.8 mmHg. L-arginine produces a statistically and biologically significant decrease in BP and improved metabolic effect in normotensive and hypertensive humans that is similar in magnitude to that seen in the DASH-I diet [Siani et al. 2000]. This reduction in BP was seen whether L-arginine was provided through natural foods or as a pharmacologic supplement when given at approximately a two-fold dietary increase (doses of 10 g per day). Although these doses of L-arginine appear to be safe, no long-term studies in humans have been published at this time and there are concerns of a pro-oxidative effect in patients who may have dysfunctional endothelium or advanced atherosclerosis, chronic heart disease or myocardial infarction.

L-carnitine
L-carnitine is a nitrogenous constituent of muscle primarily involved in the oxidation of fatty acids in mammals. Human studies on the effects of L-carnitine are small and limited with minimal to no change in BP [Digiesi et al. 1994]. Carnitine may be useful in the treatment of essential hypertension, type II DM with hypertension, hyperlipidemia, cardiac arrhythmias, CHF and cardiac ischemic syndromes.

Taurine
Taurine is a sulfonic beta-amino acid that is considered a conditionally essential amino acid, which is not utilized in protein synthesis, but is found free or in simple peptides with its highest concentration in the brain, retina and myocardium [Huxtable, 1992]. In cardiomyocytes, it represents about 50% of the free amino acids and has a role of an osmoregulator, and inotropic factor and has been used to treat hypertension [Fujita et al. 1987].

Human studies have noted that essential hypertensive subjects have reduced urinary taurine as well as other sulfur amino acids [Houston, 2007; Huxtable, 1992; Fujita et al. 1987]. Taurine lowers BP and heart rate, decreases arrhythmias, CHF symptoms and SNS activity, increases urinary sodium and decreases PRA, aldosterone, plasma norepinephrine, plasma and urinary epinephrine. A study of 31 Japanese males with essential hypertension placed on an exercise program for 10 weeks showed a 26% increase in taurine levels and a 287% increase in cysteine levels. The BP reduction of 14.8/6.6 mmHg was proportional to both taurine level elevations and plasma norepinephrine reduction [Tanabe et al. 1989].

Fujita et al. [1987] found a reduction in BP of 9/4.1 mmHg (p < 0.05) in 19 hypertension subjects given 6 g of taurine for 7 days. Taurine has numerous beneficial effects on the cardiovascular system and BP. The recommended dose of taurine is 2–3 g/day at which no adverse effects are noted, but higher doses may be needed to reduce BP significantly.

Pycnogenol
Pycnogenol, a bark extract from the French maritime pine, at doses of 200 mg/day resulted in a significant reduction in systolic BP from 139.9 to 132.7 mmHg (p < 0.05) in 11 patients with mild hypertension over 8 weeks. Diastolic BP fell from 93.8 to 92.0 mmHg (not significant). Serum thromboxane concentrations were significantly reduced (p < 0.05) [Hosseini et al. 2001]. Other studies have shown reductions in BP, reduced ET-1, reductions in HgA1C and fasting glucose and reductions in low-density lipoprotein cholesterol (LDL-C) [Zibadi et al. 2008; Liu et al. 2004].

Natural antihypertensive compounds categorized by antihypertensive class
As has been discussed previously, many of the natural compounds in food, certain nutraceutical supplements, vitamins, antioxidants or minerals function in a similar fashion to a specific class of antihypertensive drugs. Although the potency of these natural compounds may be lower than the antihypertensive drug, when used in combination with other nutrients and nutraceuticals, the antihypertensive effect is magnified. In addition,
many of these nutrients and nutraceuticals have varied, additive or synergistic mechanisms of action in lowering BP.

**Functional intracellular assessment: evaluation of the nutritional status, micronutrients, vitamins, minerals, oxidative stress and defense**

The first step that should be taken to manage hypertensive patients is a proper and accurate evaluation of their nutritional status, macronutrients, micronutrients, vitamins, minerals, vascular inflammation, oxidative stress and defense. Serum levels of many nutrients and minerals do not accurately reflect intracellular levels or long-term nutrient status. Functional intracellular measurement of micronutrients, vitamins and minerals provides a more accurate assessment of body stores and functional needs of the cell. The concept is similar to that of measurement of a single fasting glucose as opposed to measurement of the hemoglobin A1C to assess glucose control in a patient with DM. A single serum measurement of any of these tests provides only a narrow time window reflecting the nutrient intake for the previous few days rather than an average of the preceding 6 months. A careful history and detailed diary of macronutrient and micronutrient intake is important to obtain, but will not provide objective evaluation of the levels of these important nutrients in these patients. It is clear from the clinical studies presented that replacement of deficiencies of micronutrients and macronutrients as well as treatment with higher therapeutic doses of vitamins, minerals and antioxidants can lower BP as well as improve vascular health and function.

One of the best clinical assessments of nutrient, vitamin and mineral status is ‘Functional Intracellular Assessment’ [Baum et al. 2004; Boerner, 2001; Crawford, 2001; Shive, 1988; Shive et al. 1986]. The panel of tests measures selected vitamins, minerals, antioxidants and other essential micronutrients within lymphocytes giving a 6-month evaluation of nutritional status. Clinical evaluation includes vitamins A, B1, B2, B3, B6, B12, C, E, D and K2, biotin, folate, pantothenate, calcium, magnesium, zinc, copper, alpha lipoic acid, coenzyme Q 10, cysteine, glutathione, selenium, chromium, oleic acid, choline, inositol, asparagine, glutamine, serine and carnitine. In addition there is evaluation of fructose sensitivity, glucose-insulin metabolism (a measure of insulin sensitivity) and total antioxidant function (Spectrox).

Once a deficiency is noted, then adequate replacement doses of the specific micronutrient, vitamin, mineral, amino acid, antioxidant, fatty acid or metabolite is started. In addition, treatment for low antioxidant defense or abnormal glucose metabolism or insulin resistance should also be initiated. Treatment with higher therapeutic doses of selected nutrients can begin at the same time to reduce BP.

Nutritional treatment although very effective in reducing BP, may take longer than pharmacologic therapies. In some cases, it may be 4–6 months before the maximal antihypertensive effect is seen. The Functional Intracellular Assessment should be repeated in 4–6 months after initiation of treatment to evaluate adequacy of replacement therapy.

Over the past 5 years, we have incorporated this Functional Intracellular Assessment in 3338 patients in the Hypertension Institute in Nashville, TN. There were 671 hypertensive patients (BP >140/90 mmHg; BP range of up to 210 systolic and 115 diastolic) in the total population studied resulting in a 20.1% incidence. However, in the hypertensive population (n = 671) compared with the general population there were significant differences in many of the micronutrients tested as well as a significantly higher oxidative stress, a lower oxidative defense and higher incidence of insulin resistance as measured by the glucose-insulin test.

Replacement of these deficiencies as well as high-dose therapy of selected supplements and nutraceuticals in combination with optimal diet, exercise and weight management resulted in control of BP to goal levels in 62% of the hypertensive population over a period of 6 months with complete tapering and discontinuation of antihypertensive drugs. In addition, the total antioxidant functional testing (Spectrox) scores for the hypertensive patients on repeat analysis showed a statistically significant average improvement of 8.47% (p = 0.03). We also prescribed the DASH 2 diet, weight management and a combined aerobic and resistance exercise program for 60 minutes per day (see Box 4). Patient acceptance of these treatments were very high and no adverse effects were noted with the exception of occasional indigestion and mild nausea.
### Box 4. Recommendations.

<table>
<thead>
<tr>
<th>Nutrition</th>
<th>Daily Intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>DASH I, DASH II-Na+ and PREMIER diets</td>
<td></td>
</tr>
<tr>
<td>Sodium restriction</td>
<td>50–100 mmol</td>
</tr>
<tr>
<td>Potassium</td>
<td>100 mEq</td>
</tr>
<tr>
<td>Potassium/sodium ratio &gt;5:1</td>
<td></td>
</tr>
<tr>
<td>Magnesium</td>
<td>1000 mg</td>
</tr>
<tr>
<td>Calcium</td>
<td>1000 mg</td>
</tr>
<tr>
<td>Zinc</td>
<td>25–30 mg</td>
</tr>
<tr>
<td>Protein: total intake (30% total calories)</td>
<td>1.0–1.8 g/kg</td>
</tr>
<tr>
<td>Nonanimal sources preferred but lean or wild animal protein in moderation is acceptable</td>
<td></td>
</tr>
<tr>
<td>Hydrolyzed whey protein</td>
<td>30 g</td>
</tr>
<tr>
<td>Soy protein (fermented is best)</td>
<td>30 g</td>
</tr>
<tr>
<td>Sardine muscle concentrate extract</td>
<td>3 mg</td>
</tr>
<tr>
<td>Cold water fish, fowl poultry</td>
<td></td>
</tr>
<tr>
<td>Fats: 30% total calories</td>
<td></td>
</tr>
<tr>
<td>Omega-3 fatty acids PUFA</td>
<td>2–3 g</td>
</tr>
<tr>
<td>(DHA, EPA, cold water fish)</td>
<td></td>
</tr>
<tr>
<td>Omega-6 fatty acids PUFA</td>
<td>1 g</td>
</tr>
<tr>
<td>(canola oil, nuts)</td>
<td></td>
</tr>
<tr>
<td>Omega-9 fatty acids MUFA</td>
<td></td>
</tr>
<tr>
<td>(extra virgin olive oil) (olives)</td>
<td></td>
</tr>
<tr>
<td>Saturated FA (lean, wild animal meat) (30%)</td>
<td></td>
</tr>
<tr>
<td>P/S ratio (polyunsaturated/saturated) fats &gt;2.0</td>
<td></td>
</tr>
<tr>
<td>Omega-3/Omega-6 PUFA, ratio 1:1–1:2</td>
<td></td>
</tr>
<tr>
<td>No trans fatty acids [0%]</td>
<td></td>
</tr>
<tr>
<td>[hydrogenated margarines, vegetable oils]</td>
<td></td>
</tr>
<tr>
<td>Nuts: almonds, walnuts, hazelnuts, etc.</td>
<td></td>
</tr>
<tr>
<td>Carbohydrates (40% total calories)</td>
<td></td>
</tr>
<tr>
<td>Reduce or eliminate refined sugars and simple carbohydrates</td>
<td></td>
</tr>
<tr>
<td>Increase complex carbohydrates and fiber</td>
<td></td>
</tr>
<tr>
<td>whole grains [oat, barley, wheat]</td>
<td></td>
</tr>
<tr>
<td>vegetables, beans, legumes</td>
<td></td>
</tr>
<tr>
<td>i.e. oatmeal or</td>
<td>60 g</td>
</tr>
<tr>
<td>oat bran (dry) or</td>
<td>40 g</td>
</tr>
<tr>
<td>beta-glucan or</td>
<td>3 g</td>
</tr>
<tr>
<td>psyllium</td>
<td>7 g</td>
</tr>
<tr>
<td>Any one of these</td>
<td></td>
</tr>
<tr>
<td>Garlic</td>
<td>4 cloves/4 g</td>
</tr>
<tr>
<td>Nutrition</td>
<td>Daily Intake</td>
</tr>
<tr>
<td>Wakame seaweed (dried)</td>
<td>3.0–3.5 g</td>
</tr>
<tr>
<td>Any one of these</td>
<td></td>
</tr>
<tr>
<td>Lycopene</td>
<td>10 mg</td>
</tr>
<tr>
<td>Tomatoes and tomato products,</td>
<td></td>
</tr>
<tr>
<td>guava, watermelon, apricots,</td>
<td></td>
</tr>
<tr>
<td>pink grapefruit, papaya</td>
<td></td>
</tr>
<tr>
<td>Exercise</td>
<td></td>
</tr>
<tr>
<td>Aerobically</td>
<td></td>
</tr>
<tr>
<td>60 minutes daily</td>
<td></td>
</tr>
<tr>
<td>4200 kJ/week</td>
<td></td>
</tr>
<tr>
<td>Resistance training 3x/week to daily</td>
<td></td>
</tr>
<tr>
<td>Weight Loss</td>
<td></td>
</tr>
<tr>
<td>To ideal body weight (IBW)</td>
<td></td>
</tr>
<tr>
<td>Lose 1–2 pounds/week</td>
<td></td>
</tr>
<tr>
<td>BMI &lt;25</td>
<td></td>
</tr>
</tbody>
</table>

[continued]
with some nutraceuticals (3.8%). It is important to note that successful repletion of micronutrient deficiencies had a major contribution to clinical success. A greater than 97% repletion rate was observed upon retesting in the hypertensive population. In addition, antioxidant defense improved by 8.4% (p = 0.03) and there was significant improvement in lymphocyte cellular proliferation (increased by 21.2%; p = 0.015), which is a measure of cell-mediated immune function, was noted in the repeat population resulting in improvement in overall cell function and in health and wellness.

The health and economic implications of this data are enormous. The annual cost of antihypertensive drug therapy in the US in 2004 was about US$15 billion with an anticipated increase to about US$20 billion [Spurgeon, 2004]. This represents about 10% of the country’s total spending on drugs. The widespread use of Functional Intracellular Assessment with proper nutrient replacement and treatment along with life style modification could dramatically reduce the need for pharmacologic therapies and reduce adverse effects. Reductions in BP with this lifestyle program should result in major cardiovascular event reductions including MI, stroke, CHF and renal disease in the US. The cost savings related to these reductions would be huge.

Summary and conclusions

- Vascular biology (ED and VSMD) plays a primary role in the initiation and perpetuation of hypertension, 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 CVD.
- Antioxidants can prevent and treat hypertension.
- Whole food and phytonutrient concentrates of fruits, vegetables and fiber with natural combinations of balanced phytochemicals, nutrients, antioxidants, vitamins, minerals and appropriate macronutrients and micronutrients are generally superior to single component or isolated artificial or single

---

**Box 4. Continued**

<table>
<thead>
<tr>
<th>Nutrition</th>
<th>Daily Intake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist circumference</td>
<td>&lt;35 inches in female</td>
</tr>
<tr>
<td>Total body fat</td>
<td>&lt;40 inches in male</td>
</tr>
<tr>
<td>Increase lean muscle mass</td>
<td>&lt;16% in males</td>
</tr>
<tr>
<td>Alcohol Restriction</td>
<td>&lt;20 g/day</td>
</tr>
<tr>
<td>Wine</td>
<td>&lt;10 ounces [preferred: red wine]</td>
</tr>
<tr>
<td>Beer</td>
<td>&lt;24 ounces</td>
</tr>
<tr>
<td>Liquor</td>
<td>&lt;2 ounces (100 proof whiskey)</td>
</tr>
<tr>
<td>Caffeine Restriction</td>
<td>&lt;100 mg/day</td>
</tr>
<tr>
<td>Tobacco and Smoking</td>
<td>Stop</td>
</tr>
<tr>
<td>Avoid drugs and interactions that increase BP</td>
<td></td>
</tr>
<tr>
<td>Vitamins, antioxidants and nutraceutical supplements</td>
<td>Daily Intake</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>250–500 mg BID</td>
</tr>
<tr>
<td>Vitamin E (mixed tocopherol/tocotrienols)</td>
<td>400–800 IU QD</td>
</tr>
<tr>
<td>Vitamin B6</td>
<td>100 mg QD to BID</td>
</tr>
<tr>
<td>Coenzyme Q-10</td>
<td>60 mg QD to BID</td>
</tr>
<tr>
<td>Lipoic acid [with Biotin]</td>
<td>100–200 mg BID</td>
</tr>
<tr>
<td>L-carnitine</td>
<td>1000 mg BID</td>
</tr>
<tr>
<td>Taurine</td>
<td>1.0–1.5 g BID</td>
</tr>
<tr>
<td>L-arginine (food and supplements)</td>
<td>5 g BID</td>
</tr>
<tr>
<td>L-arginine (food and supplements)</td>
<td>250 mg QD</td>
</tr>
<tr>
<td>Trans Resveratrol</td>
<td></td>
</tr>
</tbody>
</table>
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, alcohol and caffeine restriction as well as other changes in lifestyle must be incorporated.

- Evaluation of nutritional and nutrient status should be done using Functional Intracellular Assessment followed by replacement therapy of deficiencies as well as utilization of higher doses of selected micronutrients to reduce BP, correct oxidative defense, improve cell function, improve cell-mediated immune function, replete all intracellular nutrient deficiencies, improved insulin sensitivity and clinical parameters of health and wellness. Sixty two per cent of patients treated with micronutrient replacement in combination with optimal diet, exercise and weight management had their BP reduced to goal levels (≤120/80 mmHg) over 6 months allowing for tapering and discontinuation of antihypertensive drug therapy (p < 0.01). The annual cost savings for this type of integrative treatment of hypertensive patients could be as much as US$10 billion.

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Conflicts of Interest

Dr Houston is a paid Speaker and Lecturer and a paid Consultant for Spectracell Research Laboratories in Texas.

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Houston (1994).


Houston (2008).


