

Hypertension

Clinically proven natural alternatives for treating high blood pressure

CURT HENDRIX, M.S., C.C.N., C.N.S.

Evidence-Based Use of Supplements

ABSTRACT

Hypertension is a leading cause of death in the United States and worldwide. It is a condition considered strongly linked to lifestyle, as it can be prevented or delayed through healthy habits that include strategic diet and exercise programs. Nonetheless, people often resort to the use of prescription drugs to manage hypertension and often suffer unwanted side effects as a result. This paper provides an overview of hypertension and its management and proposes the use of an integrative approach that combines specific lifestyle choices the use of nutraceuticals to maintain a healthy blood pressure. Specifically, the paper argues for the benefits of supplementing a healthy lifestyle with the following substances at clinically meaningful doses: hibiscus sabdariffa extract, olive leaf extract, celery seed extract, grape seed extract, and melatonin.

Higher blood pressure is associated with increased vascular and overall mortality.¹ The risk for hypertension varies by population subgroups as well as by gender, race, and age. A recent meta-analysis of risk prediction models for hypertension found that age, sex, body mass index (BMI), baseline blood pressure, and cigarette smoking were the most common predictors of high blood pressure.²

Hypertension is more prevalent in older adults, men, and African Americans. Hypertension is more prevalent in men than women before age 65 years. In older age groups, however, it is more prevalent in women.

A consensus of international data shows that BMI has a strong influence on the incidence and risk of hypertension.^{3–5}

Any blood pressure (BP) above the optimal level of less than 120/80 mm Hg carries a graded risk of advancing to high blood pressure. Persons closest to the threshold for a diagnosis of hypertension, and persons with high-normal blood pressure of 130–139/85–89 mm Hg have the highest risk.⁶

Recent evidence has revealed the instability of single blood pressure measurements and the need for multiple, valid measurements to assess a person's actual elevated blood pressure exposure. The popularity of using blood pressure kiosks found in drug stores and shopping malls has been increasing over the past decade, but there are few data available to support the use of BP kiosks, and their results are considered too variable and insufficiently researched to be included in any major guidelines.^{7,8} The recent recognition of the impact of overdiagnosis in many diseases, the widespread availability of automated blood pressure devices with variable performance, and the prevalence of essential hypertension in the United States has led to a search for alternate ways to achieve healthy blood pressure.

Dietary, lifestyle strategies, and nutraceutical use have growing evidence to support their efficacy as blood pressure control strategies. These strategies can be as effective as medications and, in some cases, even more effective.⁹

Conventional antihypertensives are often associated with many side effects. About 80% of the world's population uses herbal medicines for primary health care because of their better acceptability and lower side effects. In the last thirty years, considerable efforts have been devoted to researching indigenous plants with hypotensive and antihypertensive properties.¹⁰

Hypertension is one of the more easily controllable risk factors, but we must understand the side effects of prescription drugs, and the effective dosages of nutraceuticals as an alternative to prescription drugs. Numerous supplement companies are selling products that are pixie-dust formulations with minimal amounts of active ingredients. The old saying is true in the supplement business – *let the buyer beware*.

The more common prescription drugs for hypertension include beta blockers, angiotensin-converting enzyme (ACE) inhibitors, diuretics, alpha blockers, and calcium channel blockers. One side effect of diuretics is that the body's potassium stores are carried out of the body in the urine along with the sodium. This loss of potassium can lead to muscle cramping and in extreme cases, death. Beta blockers reduce the pumping force of the heart. Typical side effects include bradycardia (slow heart beat), cold extremities, postural hypotension (dizziness when standing), vertigo and leg pain. The most common side effects of ACE inhibitors include cough, dizziness, headache, low blood pressure and fatigue. Common calcium channel side effects include swelling, fluid in the lungs, headache, fatigue, and palpitations.

The differences between nutraceutical side effects and prescription drug side effects to lower blood pressure are dramatic. The side effects of nutraceuticals from Hibiscus, olive leaf, celery extract, grape seed extracts and melatonin are rare, but usually involve minor gastrointestinal side effects that are usually transitory. The side effects seen with prescription drugs are serious but are not reported in people taking nutraceutical blood pressure supplements. While prescription hypertension drugs can cause hypotension (low

blood pressure), nutraceuticals do not – they lower blood pressure to normal ranges but do not lower them to subnormal, dangerous ranges.

An Integrative Approach in Treating High Blood Pressure

An integrative approach combining lifestyle and nutraceuticals will best achieve healthy blood pressure levels and improve vascular health.^{11,12} Significant effects on blood pressure have been reported from large nutritional interventions, particularly the Dietary Approaches to Stop Hypertension (DASH) and the Mediterranean Diet.^{13,14} In more recent years, numerous studies have investigated the possible blood pressure-lowering effect of nutraceuticals.^{15–20}

Hibiscus Sabdariffa Extract

Hibiscus sabdariffa is an annual or perennial herb with flowers, leaves and a red calyx at its base that supports the petals of the flower. The active principals of Hibiscus, the anthocyanins and flavones are extracted from the flowers and the calyx and provide potent antioxidants, healthy blood pressure support, and positive effects on cholesterol and other blood lipids. HS decoctions, infusions of calyxes, and leaves, are used in at least 10 countries worldwide in the treatment of blood pressure and hyperlipidemia issues with no reported adverse events or side effects.²¹

A human study was conducted in 2015 in Nigeria involving 75 patients divided into three groups, Hibiscus calyx solution (a beverage in Nigeria) was prepared by boiling the calyx in water and drinking the infusion. Blackcurrant extract was used in a placebo group and the drug lisinopril was given to an active control group. The group given *Hibiscus sabdariffa* achieved a 76% improvement in healthy blood pressure at the end of week two compared to lisinopril with a 65% improvement, which only occurred at the end of week four. Three subjects in the Lisinopril group developed a cough and were placed on a different prescription medication. The mean differences between the Hibiscus and the Lisinopril active groups were not considered significantly different at the end of the trial.²²

The same researchers who conducted the 2015 clinical study, conducted another study in November and December that same year testing what effects *Hibiscus sabdariffa* and hydrochlorothiazide had on 80 patients recently diagnosed with mild to moderate out of range blood pressure. The patients were divided into three groups, a placebo group, a hydrochlorothiazide group, and a *Hibiscus sabdariffa* beverage group. HS was a more effective blood pressure normalizing agent than hydrochlorothiazide and did not cause electrolyte imbalance, unlike hydrochlorothiazide. *Hibiscus sabdariffa* was more effective than the drug and “showed a longer duration of action compared to hydrochlorothiazide. “The reduction in serum sodium may be another mechanism of action of HS.”²³

A 2007 human trial using an extract of the calyxes of *Hibiscus sabdariffa* compared it with the effects of lisinopril on patients with unhealthy blood pressure. The study enrolled patients of either sex, 25 – 61 years of age, and treated them for four weeks with the HS extract or with 10 milligrams (mg) of lisinopril used as a control group. The group treated with the *Hibiscus sabdariffa* extract had 65% healthier blood pressure, better than the lisinopril group, had lower ACE levels (Angiotension Converting Enzyme), and lower sodium levels without affecting potassium levels. *Hibiscus sabdariffa* had “a wide margin of safety and tolerability.”

One other benefit of Hibiscus sabdariffa is that half of the randomized clinical trials testing it demonstrated that

supplementation with Hibiscus sabdariffa supported healthy blood lipids with a reduction in total cholesterol, LDL-(bad)-Cholesterol, and an increase in HDL-(good)-Cholesterol. It is not common to see a natural compound or extract elevate HDL-(good)-Cholesterol.^{21,24–26}

The effective dose of Hibiscus sabdariffa used in several clinical trials is an extract standardized to 250 mg of total anthocyanins total daily dose. Any dose less than that would probably be inadequate for blood pressure-lowering blood effects.

Olive Leaf Extract

Plant polyphenols have been shown to favorably modify several cardiovascular risk markers such as blood pressure, artery and vascular function and blood serum lipids. A study using an olive leaf extract standardized to Oleuropein was used in 60 persons with borderline poor blood pressure health. The study also measured olive leaf extracts’ effects on their blood lipid (cholesterol) health. In the active olive leaf group their 24-hour blood pressure health was significantly improved, including systolic blood pressure and diastolic blood pressure relative to the group given a placebo. According to the study authors, “The magnitude of BP changes observed here can be considered physiologically significant.”¹⁶

A double-blind, randomized clinical study was conducted to compare the blood pressure health effects of olive leaf extract with the drug Captopril in persons with borderline-poor blood pressure health. Evaluation of BP was performed every week for eight weeks of the treatments. After eight weeks of treatment, both groups experienced a significant health improvement in systolic as well as diastolic blood pressure. Blood pressure improvements were not significantly different between the olive leaf extract group or the Captopril group.²⁷

Olive leaf extract was tested in an open label study of 40 twins who had borderline poor blood pressure health. Twins of each pair were assigned to two groups at different doses of the olive leaf extract for 8 weeks. Blood pressure changed significantly with significant healthy changes in systolic blood pressure and diastolic blood pressure. After 8 weeks, mean blood pressure in a control group remained unchanged. Cholesterol levels decreased in all active olive leaf extract groups, especially with LDL-(bad)-Cholesterol levels.²⁸ Olive leaf extract has a dual benefit of supporting healthier blood pressure and healthier blood lipid levels.

Olive leaf extract helps block endothelial dysfunction at various levels. Olive leaf extracts increase the production of nitric oxide necessary for blood vessel relaxation.²⁹ Olive leaf extract also reduces the production of matrix metalloproteinases that increase artery inflammation and slows the oxidation of LDL-(bad)-Cholesterol, the earliest events in hardening of the arteries.^{30–32} Oxidized LDL triggers inflammation, further damaging arteries, and olive leaf extract has multi-targeted anti-inflammatory effects.^{33,34}

The effective average dose of olive leaf extract in clinical trials is 136 mg of oleuropein as a total daily dose. Any dose less than that would have questionable results.

Celery Extract Standardized to 3-N-Butylphthalide

3-N-butylphthalide, or 3nB, is a natural compound found in celery seeds. It has multiple health benefits, including brain cell protection, inhibiting red blood cell platelet aggregation, restoring mitochondrial function and integrity (the organelles that produce cellular energy), and helping to

organelles that produce cellular energy), and helping to prevent blood flow interruption that leads to massive free radical production and ensuing damages tissues.^{35–37} A series of Chinese clinical trials have demonstrated that celery juice or celery seed extract rich in 3nB significantly restores healthy blood pressure in humans.¹⁰

Celery seed extract has potent calcium channel blocking properties, which is partly responsible for its blood pressure health-promoting properties.^{38,39}

A human clinical trial demonstrating the effectiveness of a celery seed extract standardized to 3nB was recently published in the *Natural Medicine Journal* in 2013. Thirty middle-aged patients with moderately poor blood pressure health were given a celery seed extract twice daily for six weeks. Celery seed extract significantly improved systolic blood pressure and diastolic blood pressure health at week three compared to the before-study measurements. After six weeks of consumption, the celery extract further improved systolic blood pressure and diastolic blood pressure health to normal levels.¹⁹

Prescription calcium channel blockers and ACE inhibitors are known to reduce blood flow to the brain, causing side effects of tiredness, depression, dizziness, or forgetfulness in patients. However, celery seed extracts rich in 3nB improve blood flow to the brain.^{40,41} Another benefit using celery seed extract seen experimentally is that it has no effect on normal, healthy blood pressure, unlike prescription channel blockers and ACE inhibitors. The study stated that “the celery extracts had no effect on blood pressure in normotensive groups.” The study also stated that celery extract was effective in “promoting the establishment of collateral circulation, enhancing cerebral blood flow, protecting the mitochondria, and improving the cerebral energy metabolism.”⁴²

An earlier study with 37 patients (20 female, 17 male) between the ages of 45–65 years old with poor blood pressure health were given celery seed powder for six weeks and their blood pressure health before and after treatment was compared. The difference of blood pressure before and after treatment was statistically significant. The study authors concluded that *Apium graveolens* seed can be used as a safe and effective treatment for poor blood pressure health.⁴³ The average daily effective dose of celery extract used in successful clinical trials is 150 mg per day of celery seed extract containing 85% 3nB (3-N-butylphthalide). Synthetic 3nB is being developed as a drug in China, so beware of products containing synthetic 3nB.

Grape Seed Extract

Grape seed extract is effective at restoring healthy blood pressure in numerous human clinical trials. A 2016 meta-analysis of sixteen clinical trials involving 810 subjects demonstrated grape seed’s ability to produce healthy changes in systolic blood pressure and diastolic blood pressure after grape seed extract treatment in younger subjects, older subjects, or persons with metabolic syndrome. The meta-analysis stated that “The key finding of this study was that grape seed extract exerted a beneficial impact on blood pressure, and this impact was more obvious in younger or obese subjects, as well as in patients with metabolic disorders. As far as we know, this is to date the argest meta-analysis that has evaluated the relationship between grape seed extract treatment and blood pressure changes.” The authors also stated that there was no indication of publication bias in any of the studies reviewed.¹⁷

One mechanism of action of grape seed extract is its ability to relieve oxidative stress. Oxidative stress is the imbalance between free radical production and the body’s ability to quench free radicals efficiently.^{44,45} Grape seed also increases nitric oxide levels in artery endothelial cells.⁴⁶ The added benefits of grape seed supplementation are that it increases flow-mediated dilation of blood vessels, lowers heart rate, and slows the oxidation of LDL-(bad)-Cholesterol, the earliest initiating step in atherosclerosis.^{47–49} The average effective dose of grape seed extract used in clinical trials is 300 mg per day.

Melatonin

Melatonin is a hormone released by the pineal gland but is also obtained through the diet. It a potent antioxidant, anti-inflammatory factor, and an immune modulator. It also contributes to regulating the circadian system that controls sleep and wakefulness, shows benefits on cardiovascular functions, and helps maintain healthy blood pressure.⁵⁰ Melatonin has been substantiated as an effective and safe blood pressure support agent.^{51–53} Melatonin receptors have been identified within the central and peripheral nervous system, as well as the cardiovascular system. Recent research has emerged highlighting a key role of melatonin in the automatic (autonomic) regulation of blood pressure.

In human studies, melatonin administration demonstrates clinically significant results in regulating unhealthy blood pressure.^{51–54} People who do not produce sufficient melatonin at night have unhealthy blood pressure levels during the night.⁵⁵ Volunteers given melatonin supplements during the day have shorter sleep onset at night.⁵⁶

The precise mechanism by which melatonin elicits its blood pressure health effects in humans is still poorly understood. The potential mechanisms behind the blood pressure health effects of melatonin include artery-dependent vasodilation, antioxidant effects, blocking enzymes that break down nitric oxide and improving mitochondrial function.^{57–59} The clinical effective doses used with melatonin in more recent studies of the past decade use between 2.5 mg to 5 mg of melatonin taken before bedtime to reduce nocturnal blood pressure.

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Conclusion

Natural supplements are an effective way to achieve and maintain healthy blood pressure to avoid the side-effects of prescription drugs. Combinations of plant extracts and nutrients tested in numerous human trials to support healthy blood pressure, promote circulatory health, and provide antioxidant protection for the artery endothelial cells that are most vulnerable to free radical damage. Hibiscus sabdariffa extract standardized to anthocyanins has been directly tested against two different blood pressure drugs with better results and no loss of key electrolytes. Olive leaf extract favorably affects cardiovascular risk markers such as blood pressure, artery function and blood serum lipids, helps prevent LDL-(bad)-Cholesterol oxidation, and is equal to a prescription drug in supporting healthy blood pressure. Celery seed extract standardized to 3nB improves blood flow to the brain while supporting healthy blood pressure. Celery seed has no effect on normal blood pressure, unlike prescription channel blockers and ACE inhibitors. Celery seed protects the mitochondria, and improves cerebral energy metabolism, something that prescription drugs do

not do.

Grape seed extract is so effective in supporting healthy blood pressure, it has been the subject of several meta-analyses of clinical trials supporting its effectiveness. Grape seed extract is a potent antioxidant, restoring and protecting nitric oxide levels in circulatory cells for better vasodilation. Melatonin plays a key role in blood pressure health by being an automatic regulator of it, controlling artery dilation, preventing nitric oxide depletion, and restoring low levels of melatonin at night for better blood pressure control.

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