### Natural Approach to Hypertension

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#### Abstract

Hypertension is a common problem facing many Americans today, with two million new cases being diagnosed each year. Although billions of dollars are spent annually in the United States for the treatment and detection of cardiovascular disease, current conventional treatments have done little to reduce the number of patients with hypertension. Alternative medicine offers an effective way to decrease the rising number of people with high blood pressure. Research has found a variety of alternative therapies to be successful in reducing high blood pressure including diet, exercise, stress management, supplements, and herbs.

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#### Introduction

Hypertension is one of the leading causes of disability or death, due to stroke, heart attack, and kidney failure. Expenses related directly or indirectly to the treatment and detection of hypertension in the United States are approximately \$10 billion yearly. Heart disease and stroke remain the first and third leading causes of death, respectively, in the United States. Despite the importance of these observations, for many people blood pressure is poorly controlled.<sup>1</sup>

An estimated 50 million American adults (25 percent of all adults) have high blood pressure, but only 68 percent are aware of their condition, and only 27 percent have it under control.<sup>2</sup> Each year, two million new cases of hypertension are diagnosed.<sup>3</sup> The risk of hypertension increases with age in both men and women.<sup>4</sup> Before age 55, more men than women have hypertension; the reverse is true for those over the age of 55. African Americans have significantly more risk of developing high blood pressure then Caucasians and Mexican Americans.

There are two types of high blood pressure: essential (primary) hypertension and secondary hypertension. Essential hypertension does not have a readily identifiable cause, and is the most common type of hypertension, accounting for 90 percent of all cases of high blood pressure. Genetics play a major role in essential hypertension. In the case of secondary hypertension, the cause can be identified and is usually treatable or reversible.

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**Table 1.** Conventional Anti-Hypertensive Drug Categories

Diuretics - decreasing blood volume

ACE inhibitors – reduce the production of angiotensin (a substance which causes arteries to constrict)

Beta-blockers – block the effects of epinephrine, resulting in vasodilation

Calcium-channel blockers – decrease the contractions of the heart and enhance vasodilation

Optimal blood pressure (BP) is 120/80 mm Hg or less. The systolic pressure measures the force that blood exerts on the artery walls as the heart contracts to pump blood, while the diastolic pressure measures the force when the heart relaxes to allow blood flow into the heart.

Table 1 outlines the conventional guidelines for drug therapy.<sup>6</sup> Beta-blockers, diuretics, or both are usually the first line of treatment for most physicians.<sup>7</sup>

### Dietary Approaches to Hypertension

A diet low in saturated fat and high in complex carbohydrate is recommended. Such a diet includes whole grains, fruits, vegetables, nuts, seeds, legumes, fish, soy products, onions, garlic, foods rich in potassium, calcium, and magnesium (carrots, spinach, celery, alfalfa, mushrooms, lima beans, potatoes, avocados, broccoli, and most fruits), and restricts salt.

Subjects (n=133) were enrolled in the Dietary Approaches to Stop Hypertension (DASH) trial in order to determine the effect of diet on blood pressure. Systolic blood pressures of participants ranged from 140-159 mm Hg, while diastolic BPs were 90-95 mm Hg.

Subjects ate a control diet for three weeks before being randomized to receive either a diet rich in fruits and vegetables, that same diet but with elimination of red meat, sugar, and reduced in fats, or a control diet for another eight weeks. The low-fat, lowsugar diet rich in fruits and vegetables significantly reduced both systolic and diastolic BP. While the fruits-and-vegetables diet also significantly reduced systolic and diastolic blood pressures, the combination diet produced greater BP-lowering ef-

fects; changes were evident within two weeks of starting the diet. By the end of the eightweek trial, 70 percent of participants eating the combination diet had a systolic BP less than 140 mm Hg and diastolic BP less than 90 mm Hg, compared with 45 percent on the diet rich in fruits and vegetables and 23 percent on the control diet.<sup>8</sup>

#### **Lifestyle Changes**

More than one-third of the adult population of the United States is obese,<sup>9</sup> presenting a significant risk factor for hypertension. Many studies have shown obese hypertensive patients can reduce their medication with weight loss. A sedentary individual has a 35-percent greater risk of developing hypertension than does an athlete.<sup>6</sup>

One study found insufficient sleep can contribute to increased blood pressure in hypertensives. The researchers theorized this may be due to increased sympathetic nervous activity during the night.<sup>10</sup>

Stress management and relaxation techniques such as meditation can help in controlling high blood pressure. In one study researchers found nearly 70 percent of patients with mild to moderate hypertension using techniques to reduce stress were able to reduce

their medication after six weeks; after one year, 55 percent required no medication.<sup>11</sup>

#### **Specific Nutrient Supplementation**

## Minerals: Potassium and Magnesium

Potassium is one of the most important minerals for hypertension. It is well documented that a diet low in potassium and high in sodium is associated with hypertension. 12-17

There have been several studies indicating magnesium (Mg) may help to lower blood pressure and even prevent hypertension. Its hypotensive effect is thought to be due to relaxation of the smooth muscles of the blood vessels. A recent study demonstrated magnesium supplementation prevented blood pressure elevation in hypertensive rats. Magnesium's mechanism of action was theorized to be associated with inhibition of platelet calcium uptake and decrease in intracellular free calcium concentrations.<sup>18</sup> In another study, researchers showed that taking magnesium in amounts as low as 365 mg per day with beta blockers can significantly reduce blood pressure compared to taking beta blockers alone.19

In a double-blind cross-over study of magnesium in hypertension, 17 subjects (diastolic BPs > 90 mm Hg) were supplemented with 15 mM Mg daily for three weeks, 30 mM Mg for another three weeks, and ending with 40 mM Mg for a final three weeks. Statistically significant decreases in average systolic and diastolic BPs were noted.<sup>20</sup>

#### Coenzyme Q10

Studies have clearly shown the potential benefit of coenzyme Q10 (CoQ10) in treatment of hypertension and congestive heart failure. <sup>21-25</sup> In one study, 109 patients with essential hypertension were supplemented with CoQ10 at an average oral dose of 225 mg/day in addition to their existing antihypertensive

drug regimen. Eighty percent of patients in the study had been diagnosed with hypertension for an average of 9.2 years. Dosage was dependant on blood levels of CoQ10, the objective being to maintain blood levels of greater than 2.0 mcg/mL. Patients were gradually able to decrease antihypertensive drug therapy during the first one to six months. Fifty-one percent of patients were able to completely discontinue between one and three antihypertensive drugs an average of 4.4 months after starting CoQ10.<sup>26</sup>

In addition to normalizing blood pressure, another study found that CoQ10 may also be effective in reducing total cholesterol. In this study 26 hypertensives were supplemented with CoQ10 at a dose of 50 mg twice daily for 10 weeks. Plasma CoQ10, serum total and HDL cholesterol, and blood pressure were determined in all patients before and at the end of the 10-week period. At the end of the treatment, systolic blood pressure decreased from an average of 164 mm Hg to 146 mmHg, while diastolic blood pressure decreased from an average of 98 mm Hg to 86 mm Hg. Average serum total cholesterol decreased slightly, from 222 mg/dL to 213 mg/dL, while there was no significant change in HDL levels.<sup>27</sup> Long term studies on safety of CoQ10 have shown it to be a safe supplement.<sup>22</sup> It may take as long as 4-12 weeks to note significant results.

#### **Omega-3 Fatty Acids**

Increasing the intake of omega-3 fatty acids can lower blood pressure.<sup>28</sup> Recent research suggests that the omega-3 fatty acid, eicosapentanoic acid (EPA), directly modulates intracellular calcium ion (Ca2+) signaling in vascular smooth muscle cells, resulting in a vasodilation effect and lowering of blood pressure.<sup>29-31</sup>

Sixteen mild essential hypertensive male outpatients and 16 normotensive male controls were randomly assigned to receive either EPA and docosahexanoic acid (DHA) (2.04 g EPA and 1.4 g DHA) or olive oil (4 g/day) as a placebo for a period of four months. The effect of omega-3 fatty acids on blood pressure in the treatment group was maximized after two months with systolic BP decreasing an average of 6 mm Hg, (p<0.05) and diastolic blood pressure down an average of 5 mm Hg, (p<0.05).<sup>32</sup> Omega-3 oils are also effective in lowering triglycerides and LDLs, and increasing HDLs.

In a double-blind placebo-controlled study of 935 patients with hypertriglyceridemia and hypertension, researchers found omega-3 oil supplementation resulted in significant reductions in total cholesterol and blood pressure and significant increase in HDL (an overall mean rise of 7.4 percent).<sup>33</sup> In addition, omega-3 oils can prevent primary or secondary coronary heart disease.<sup>34-37</sup>

### Amino Acids: L-Arginine and Taurine

L-arginine is a precursor to nitric oxide (endothelial-derived relaxing factor) which dilates blood vessels and lowers blood pressure. Several studies have shown that inhibiting the synthesis of nitric oxide in animal models results in hypertension.<sup>38</sup>

Dietary L-arginine supplementation has been proposed to reverse endothelial dysfunction in certain conditions, including hypercholesterolemia, coronary heart disease, and some forms of animal hypertension. Chronic oral administration of L-arginine prevented the blood pressure rise induced by sodium chloride loading in salt-sensitive rats.<sup>39</sup>

A single-blind, controlled, crossover dietary intervention was conducted on six healthy subjects in order to assess the effects of an L-arginine enriched diet on blood pressure. The subjects randomly received three different diets, each for a period of one week: (1) a control; (2) a natural foods diet enriched with L-arginine; or (3) a diet identical to the

control diet with the addition of L-arginine supplementation. A decrease in BP was observed with both L-arginine-enriched diets. In addition, creatinine clearance was improved and fasting blood sugar decreased by the addition of L-arginine.<sup>39</sup>

Taurine, a sulfur-containing amino acid, has been reported to have antihypertensive and sympatholytic activity.<sup>40</sup> Nineteen patients with borderline hypertension were supplemented with 6 g taurine daily for seven days in a double-blind, placebo-controlled study. Systolic BP in the 10 taurine-treated patients decreased an average of 9 mm Hg compared with a 2 mm Hg decrease in the nine patients treated with placebo; diastolic BP in the taurine-treated patients decreased an average of 4 mm Hg compared with 1 mm Hg in the placebo-treated subjects. Taurine supplementation resulted in a significant decrease in plasma epinephrine but not norepinephrine levels. Individuals with hypertension tend to have higher epinephrine compared to people with normal blood pressure. 41 Research shows taurine relaxes blood vessels by enhancing endorphin production, resulting in lowered blood pressure. 42,43

#### Vitamins C and E

Vitamins C and E may both play a beneficial role in the prevention and treatment of hypertension. Vitamin C has the potential to impact defective endothelium-dependent vasodilation. Although the mechanism has not been fully elucidated, it is believed that ascorbic acid functions as an antioxidant to either enhance the synthesis or prevent the breakdown of nitric oxide. 44 A 1999 Lancet randomized, double-blind, placebo-controlled study showed that treatment of hypertensive patients with vitamin C lowered blood pressure. Thirtynine patients received either ascorbic acid (n=19) or placebo (n=20) in a one-time dose of 2 g, followed by 500 mg daily for 30 days. Mean systolic blood pressure decreased from

**Table 2.** Nutrients for Hypertension

Potassium
Magnesium
Coenzyme Q10
Omega-3 Fatty Acids
L-Argenine
Taurine
Vitamin C
Vitamin E

155 mm Hg to 142 mm Hg (p<0.001) after 30 days in the ascorbate group, while placebo had no effect. Mean diastolic BP decreased in the ascorbate group after one month but was not significantly different than placebo. There was no significant effect in blood pressure after the initial 2 g dose.<sup>45</sup>

Vitamin E has also been found to increase nitric oxide synthase activity, resulting in lowered blood pressure in hypertensive patients. An animal study found that for all alpha-tocopherol-treated groups, blood pressure was significantly reduced compared to a hypertensive control group; maximum reduction of blood pressure was achieved at a dosage of 34 mg alpha-tocopherol/kg diet.<sup>46</sup>

Table 2 summarizes some of the important nutrients for hypertension.

#### Specific Botanicals for Hypertension Hawthorne (*Crataegus oxycantha* and monogyna)

Hawthorne has been used traditionally for cardiovascular disorders in many cultures. It contains a number of active constituents including flavonoids, catechins, triterpene saponins, amines, and oligomeric proanthocyanidins (OPCs). Hawthorne has been shown to exert a mild blood pressure lowering effect<sup>47,48</sup> that can take up to four weeks

for maximal results. It is believed that the herb dilates coronary blood vessels. 48 One *in vitro* study on rat aorta found proanthocyanidins extracted from hawthorne relaxed vascular tone via endothelium-dependent nitric oxidemediated relaxation. 49

#### Arjuna Bark (Terminalia arjuna)

Terminalia arjuna is a deciduous tree found throughout India. Its bark has been used in Ayurvedic medicine for over three centuries. Terminalia's active constituents include tannins, triterpenoid saponins, flavonoids, gallic acid, ellagic acid, OPCs, phytosterols, calcium, magnesium, zinc, and copper. Several studies have elucidated Terminalia's effects on various cardiac disorders including congestive heart failure, coronary artery disease, and hypertension. A study on its effects on stable and unstable angina patients found it effective for those with stable angina, with a 50-percent reduction in angina episodes and significant decrease in systolic blood pressure. St

In a double-blind crossover study, 12 subjects with refractory chronic congestive heart failure (idiopathic dilated cardiomyopathy (n=10); previous myocardial infarction (n=1). or peripartum cardiomyopathy (n=1)), received *Terminalia* arjuna, at a dose of 500 mg every eight hours, or placebo for two weeks, each treatment protocol separated by a two-week washout period, as an adjuvant to conventional therapy. Clinical, laboratory, and echocardiographic evaluations were carried out at baseline and at the end of therapy. Terminalia, compared to placebo, was associated with improvement in symptoms and signs of heart failure, decrease in echo-left ventricular end diastolic and end systolic volume indices, increase in left ventricular stroke volume index, and increase in left ventricular ejection fractions.<sup>52</sup> A study with similar dosing on primarily postmyocardial infarction angina patients found improvements in cardiac function. Prolonged use resulted in no adverse side effects or signs of renal, hepatic, or hematological abnormalities.<sup>53</sup>

### Olive Leaf (Olea africana and Olea europea)

Olive leaf extract is derived from the leaves of the olive tree. The entire leaf extract contains several phytochemicals, including 20percent oleuropein, a complex structure of flavonoids, esters, and multiple iridoid glycosides, which acts as a vasodilator, lowering blood pressure and preventing angina attacks. Oleuropein is also being recognized as a potent antioxidant. 54,55 The hypotensive action of olive leaf has been studied for two decades. A clinical study of *Olea europaea* L. aqueous extract was conducted on two groups of hypertensive patients, 12 patients consulting for the first time, and 18 patients on conventional antihypertensive treatment. An aqueous extract was given for three months, after 15 days of placebo supplementation. Researchers noted a statistically significant decrease of blood pressure (p<0.001) for all patients, without side effects.56

One of olive leaf's mechanisms of action is vasodilation. In an *in vitro* study a decoction of olive leaf caused relaxation of isolated rat aorta endothelium. The relaxant activity was independent of the integrity of the vascular endothelium. Oleuropeoside was found to be a component responsible for vasodilator activity; however, the researchers felt at least one other principle was either a vasodilator itself or potentiated the relaxant effect of oleuropeoside.<sup>57</sup>

#### **European Mistletoe** (Viscum album)

The use of mistletoe in medicine has become popular, not only because of its hypotensive activity, but also because of its anticancer properties. Mistletoe is known to possess hypotensive, cardiotonic, vasodilatory, antispasmodic, tumor-inhibiting, and thymus-

stimulating activity.<sup>58</sup> Its pharmacological effects, including diuretic and hypotensive activity, were studied using an alcohol extract of Japanese and European mistletoe. Both extracts showed blood pressure lowering effects when administered intravenously and orally to cats.<sup>59</sup> Other researchers have reported similar hypotensive effects of mistletoe in experimental animal studies.<sup>60</sup>

#### Yarrow (Achillea wilhelmsii)

Achillea wilhelmsii C. Koch (Asteraceae) has flavonoids and sesquiterpene lactone constituents, which have been found effective in lowering blood pressure and lipids. A double-blind, placebo-controlled trial examined the antihyperlipidemic and antihypertensive effects of Achillea. The researchers randomly selected 120 men and women, aged 40-60 years, and divided them into two groups: (1) moderate hyperlipidemic and (2) hypertensive subjects. Each study group was treated either with an alcohol extract of Achillea or placebo at a dose of 15-20 drops twice daily for six months. Blood pressure and serum lipids (total cholesterol, triglycerides, LDL-cholesterol and HDL-cholesterol) were measured at the end of two, four, and six months. A significant decrease was noted in triglycerides after two months, and significant decreases in triglycerides and total- and LDLcholesterol after four months. Levels of HDLcholesterol were significantly increased after six months' treatment. A significant decrease was observed in diastolic and systolic blood pressure after two and six months, respectively (p<0.05).<sup>61</sup> Results are outlined in Table 3.

#### Black Cumin Seeds (Nigella sativa)

Nigella sativa (Ranunculaceae) has a long history of use in folk medicine as a diuretic and hypotensive agent. In an animal study, an oral dose of either Nigella sativa extract (0.6 mL/kg/day) or furosemide (5 mg/kg/day) significantly increased diuresis by

**Table 3.** Study Results of Yarrow for the Treatment of Hypertension and Hyperlipidemia <sup>61</sup>

Variables	Yarrow group Mean ± SD (n=30)	Placebo group Mean ± SD (n=30)	p-value
Total cholesterol			
After 2 months	-0.08 ± 12.1	2.3 ± 11.1	NS
After 4 months	-31.7 ± 84.4	2.9 ± 41.2	0.04
After 6 months	$38.8 \pm 59.4$	4.6 ± 91.4	0.3
LDL-cholesterol			
After 2 months	-16 ± 45.1	2.6 ± 32.3	NS
After 4 months	-31.4 ± 32.4	$2.6 \pm 39.3$	0.001
After 6 months	-35.6 ± 42.6	$3.4 \pm 28.5$	0.0001
HDL-cholesterol			
After 2 months	17 ± 24.3	$0.7 \pm 3.6$	NS
After 4 months	17 ± 8.1	15.3 ± 5.6	NS
After 6 months	20.4 ± 9.1	-4.3 ± 8.9	<0.0001
Triglycerides			
After 2 months	-6 ± 24.3	2.9 ± 6.51	0.05
After 4 months	-67.3 ± 56.4	$8.4 \pm 64.9$	<0.0001
After 6 months	-75.3 ± 48.2	14.5 ± 52.3	<0.0001
Systolic pressure			
After 2 months	-5 ± 10.2	-2.9 ± 5.0	NS
After 4 months	-11.2 ± 9.8	-4.7 ± 13.6	NS
After 6 months	-14.1 ± 10.9	-3.8 ± 8.6	0.005
Diastolic pressure			
After 2 months	-8.3 ± 5.8	-0.6 ± 7.8	0.003
After 4 months	-16.9 ± 5.0	-1.4 ± 9.9	0.001
After 6 months	-14.7 ± 6.2	-2.6 ± 8.6	< 0.0001

Minus sign indicates decrease of factors compared to initial values.

16- and 30 percent, respectively, after 15 days of treatment. In the same rat study, a comparison between *Nigella sativa* and nifedipine found mean arterial pressure decreased by 22- and 18 percent in the *Nigella sativa* and nifedipine treated rats, respectively.<sup>62</sup>

The essential oil of *Nigella sativa* seed has an antioxidant property that makes it useful in treating cardiovascular disorders. Active constituents of *Nigella sativa* are thymoquinone, dithymoquinone, thymohydroquinone, thymol,<sup>63</sup> carvacrol, tanethole and 4-terpineol. Hypotensive action of Nigella is mainly due to its volatile oils. An animal study found the volatile oil has the

potential of being a potent, centrally acting antihypertensive agent.<sup>64</sup> Thin-layer chromatography (TLC) has confirmed Nigella's antioxidant properties.<sup>65</sup>

#### Forskolin (Coleus forskohlii)

Coleus forskohlii has been used in Ayurvedic medicine for many years. In 1974 the Indian Central Drug Research Institute discovered that forskolin, a component of this plant, has hypotensive and antispasmodic action. Forskolin's blood pressure lowering effects appear to be due to relaxation of arterial vascular smooth muscle. In a study with isolated heart tissue, forskolin activated

membrane-bound adenylatecyclase and cytoplasmic cAMP-dependent protein kinase. The researchers postulated the positive inotropic effect was via an enhanced calcium uptake by the heart muscle cell.<sup>66</sup> Another constituent from Coleus, ditermene coleonol, has been found to lower blood pressure in both rat and cat models.<sup>67</sup>

### Indian Snakeroot (Rauwolfia serpentina)

Rauwolfia is cultivated for the medicinal use of its 30 alkaloids (particularly reserpine found in the root), many used in treating hypertension.<sup>68</sup> Besides reserpine, other alkaloids used in hypertension and other cardiac disorders are ajmaline, rescinnamine, serpentinine, sarpagine, deserpidine, and chandrine. Rauwolfia alkaloids work by controlling nerve impulses along certain pathways that affect heart and blood vessels, lowering blood pressure. Rauwolfia depletes catecholamines and serotonin from nerves in the central nervous system.<sup>69</sup> In a controlled intervention trial, 389 subjects, ages 21-55 years, with diastolic blood pressures 90-115 mm Hg were examined for 7-10 years. Subjects were randomly assigned to either a combination of a diuretic and Rauwolfia serpentina, or an identical placebo. Diastolic blood pressure was reduced an average of 10 mm Hg and systolic by 16 mm Hg in the active treatment group, with no change in the placebo group.<sup>70</sup>

The Rauwolfia constituent ajmaline not only lowers blood pressure, but also has a potent antiarrhythmic effect. Studies have shown that ajmaline specifically depresses intraventricular conduction, suggesting this would be particularly effective in the treatment of re-entrant ventricular arrhythmias.<sup>71,72</sup>

In one study of 100 patients with essential hypertension, it was determined that serum cadmium levels were 43-percent higher and serum zinc levels 28-percent lower in hypertensives when compared with normotensive controls. When the patients were put on ajmaloon, a preparation from *Rauwolfia* 

serpentina, blood pressure was lowered significantly. It also appeared to decrease the elevated serum cadmium levels in these individuals.<sup>73</sup>

#### Garlic (Allium sativum)

Garlic is eaten in Asia, the Middle East, and in many other cultures on a daily basis. It is an ancient home remedy that has been used for many different purposes, including hypertension, and reduces a number of risk factors associated with cardiovascular disease including: (1) reducing total and LDL-cholesterol, (2) increasing HDL-cholesterol, (3) lowering triglycerides and fibrinogen, (4) lowering blood pressure, (5) improved circulation, (6) enhancing fibrinolysis, (7) inhibition of platelet aggregation, and (8) reducing plasma viscosity. The blood pressure effect is thought to be due to an opening of (Ca) ion channels in the membrane of vascular smooth muscle, affecting hyperpolarization, resulting in vasodilation.<sup>74</sup> A garlic preparation containing 1.3-percent allicin at a large dose (2400 mg) was evaluated in an open-label study in nine severely hypertensive patients (diastolic blood pressure

115 mm Hg or greater). Approximately five hours after taking the garlic, the systolic blood pressure fell an average of 7 mm Hg while diastolic BPdropped an average of 16 mm Hg. A significant decrease in diastolic blood pressure lasted from 5-14 hours after the dose and no significant side effects were reported.<sup>75</sup>

# **Table 4.** Botanicals for the Treatment of Hypertension

Hawthorne
Arjuna bark
Olive leaf
European mistletoe
Yarrow
Black cumin seeds
Nigella sativa
Forskolin
Indian Snakeroot
Garlic

Table 4 summarizes potential botanicals for the treatment of hypertension.

#### **Conclusion**

Lifestyle change, including diet, exercise, and stress management, may contribute significantly to lowering of blood pressure. Supplements such as potassium, magnesium, CoQ10, omega-3 fatty acids, amino acids Larginine and taurine, and vitamins C and E have been effectively used in the treatment of cardiovascular disease, including hypertension.

Botanicals have been used for centuries to treat various diseases including cardio-vascular disorders. It is no surprise they have proven effective in lowering blood pressure and improving heart function. Among the most researched and frequently utilized for hypertension are hawthorne, *Terminalia arjuna*, olive leaf, European mistletoe, yarrow, black cumin seeds, forskolin, Indian snakeroot, and garlic.

More research is indicated to determine the full potential that alternative medicine has to offer in the management of hypertension. With the increasing numbers of patients suffering from hypertension and conventional medicine failing to effectively control the problem, alternative therapies offer hope.

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