

Case study review: pharmacognosy of complementary and alternative medicines as effective adjuncts in the treatment of mild to moderate hypertension

Abstract

The applications of Complementary and Alternative medicine strategies using naturally occurring plants and plant products have played an important role in the treatment and amelioration of illness and disease for hundreds if not thousands of years in many parts of the world. The practice of Traditional Chinese Medicine (TCM) includes an extensive nutraceutical formulary with its origins dating back for over 2,000 years, and in North American and other indigenous societies the use of locally available naturally occurring plants contributed to the prevention of numerous nutritional deficiencies including scurvy. In European cultures, and in Central and South American societies the use of natural products also contributed an important role in their health and wellbeing. In the Caribbean, the earliest populations arose from migrating from indigenous peoples from South and Central America with later immigrants arriving from Europe and the African continent, bringing with them the plants and animals that were important to their respective cultures to add to the local environments. This resulted in the abundance of nutraceutical related plants throughout the region, and that the Caribbean now hosts one of the most diverse and extensive arrays of medicinal plants known to exist on the planet. In the present editorial we will review the Pharmacognosy and use of TCM and CAM strategies with practices originating in China and the Caribbean region respectively as compared to allopathic medications on the treatment of mild to moderate intensity hypertension.

Keywords: obesity, hypertension, traditional chinese medicine, mango leaf+ginger tea, systolic blood pressure (SBP), diastolic blood pressure (DBP), pharmacognosy

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Abbreviations: TCM, traditional chinese medicine; MLT, mango leaf tea; MGT, mango leaf + ginger tea; NIDDM, Non insulin dependent diabetes mellitus; T2DM, Type II Non-insulin dependent diabetes mellitus; HTN, hypertension, elevated blood pressure (>140/80); SWT/SWT formula, wu cao si wu tang formula; WCSWT formula, Wu Cao Si Wu Tang formula; ARs, beta (β)-adrenergic receptors; Calcium channel blocker agents, allopathic pharmaceuticals that lower blood pressure via inhibiting the intracellular translocation of calcium ions in vascular smooth muscle

Introduction

The application of Traditional Chinese Medicine (TCM) formularies for the treatment of illness and disease represents one of the oldest recorded uses of phytotherapeutic uses of natural products. Among the various herbs and other plant sources include Yunnan Baiyo, Chaun Xin Lian Pian, Plum Fruit, Achthyrathias root, Asian plaintain root and others.¹⁻³ TCM agents may be administered in many forms, including capsules, powders, ointments, therapeutic teas, and extracts, and may be used as monotherapy or as combination therapy with other natural products or as adjuncts to conventional allopathic pharmaceuticals. Si Wu Tang is a derivative of agents found in the traditional Chinese formulary and has been used in the treatment of hypertension and cardiovascular disorders in China and abroad and is also known as the Wu Cao Si Wu Tang (or SWT formula).⁴ The constituents of the SWT formula are believed to work in a synergistic manner in the amelioration of pathophysiologic symptoms when used to treat the hypertension associated with obesity and a variety of other disorders. Because the presence of hypertension is a common

finding in obesity and is a significant risk factor for cardiovascular morbidity and mortality in addition to end stage renal disease, the application of effective, cost effective and doable strategies are important determinants in preventing and addressing the sequela of hypertension at an early stage of its development.⁵ In the Caribbean and other tropical regions the use of a tea preparation based on the phytonutrients and nutraceutically active constituents of mango leaves to form a concoction has been commonly used to treat mild to moderate hypertension, and like the SWT regimen has also proved to be an effective adjunct in treating mild to moderate hypertension as monotherapy or combination therapy in patients who may have inadvertently become refractory to an allopathic regimen.⁴ The mechanism or mechanisms of action of natural products are likely complex in nature and may impact one or more key pathophysiologic parameters in contributing to their amelioration of the hypertensive stigmata.

While the specific mechanisms of action and pharmacognosy of natural and CAM regimens are largely unknown and speculative at best as contrasted to well-studied allopathic regimens, some known general mechanisms of action may be briefly summarized as follows:

Pharmacognosy and Mechanisms of action of common antihypertensive agents of allopathic and natural origin.

Beta-adrenergic receptor blockade: Metoprolol Succinate. Beta-blocker agents are widely used molecules that are able to antagonize beta (β -adrenergic) receptors (ARs) in cardiovascular tissues and have been in wide clinical use for over 50 years due to their ability to reduce

heart rate and consequently myocardial oxygen demand in the event of an angina attack.⁶ These agents belong to the G protein-coupled receptor family and receive their stimulus from endogenous naturally occurring catecholamines including epinephrine, norepinephrine, and analogues. The concept of β -blockade originated with studies with dichloroisoproterenol by Ahlquist et al (1958) which paved the way to development of more selective analogues of AR blockade.⁶ Metoprolol succinate is a pharmacologic and nonselective beta-adrenergic receptor blocking agent, which physiologically impinges in vascular β_1 and β_2 adrenoreceptors to block the adrenergic, vasoconstrictive effects of catecholamines. Beta adrenergic blockade results in relaxation of vascular smooth muscle, thereby decreasing the magnitude of vascular resistance, and the subsequent lowering of both systolic and diastolic blood pressures. Metoprolol succinate can be prescribed as either monotherapy or in combination with other antihypertensive agents and is usually prescribed to be taken early in the day along with other medications and may be most effective if taken prior to consuming the first meal of the day.⁶

Angiotensin receptor blocker: Losartan Potassium salt. Losartan potassium is an antihypertensive agent that belongs to a class of drugs called angiotensin receptor blockers (ARBs). The ARBs bring about reductions in both systolic and diastolic blood pressure via inhibiting the hemodynamic, vasoconstrictive effects of angiotensin, a peptide which generates potent vasoconstrictor and renal sodium retention activity which can further increase blood pressure. Treatment with losartan potassium typically results in a relaxation of vascular smooth muscle and subsequent vasodilation, thereby lowering of vascular resistance such that peripheral blood flow may occur more easily and with less cardiac work product. Because of the potassium content of losartan, plasma potassium concentrations should be monitored periodically to minimize the occurrence of hyperkalemia with its potential adverse cardiac actions.⁶

Calcium Channel Blocker: Amlodipine. Amlodipine belongs to a class of antihypertension pharmacologic agents referred to as calcium channel blockers due to their unique mechanism of action. The class of Calcium channel blocking agents work by a dose-related slowing or preventing of calcium entry from plasma into the myocytes of the heart and arteries. Calcium ions enable the cardiac and vascular smooth muscle fibers to contract more strongly, thereby bring about increased tension in the peripheral vasculature, particularly in the arterial side. By blocking calcium entry, calcium channel blockers permit blood vessels to relax and undergo dilation, with a subsequent decrease in vascular pressure. Because Calcium channel inhibition facilitates a relaxation of peripheral smooth muscle fibers, it effectively decreases the magnitude of cardiac work product as a result of the peripheral vascular relaxation. Amlodipine may be used alone as monotherapy or in combination with other medications to treat hypertension in adults and youth over the age of 6 years. This agent can also be used to treat certain types of angina and coronary artery disease caused by narrowing of the coronary blood vessels if administered prior to the onset of the anginal pain. Accordingly, it can help to control symptoms of anginal chest pain associated with constriction of the coronary vessels by increasing the supply of blood and thus oxygenation to the heart muscle. If taken regularly, along with regular modest exercise, amlodipine can control the onset of most anginal pain and discomfort, but it is typically most effective if taken before the onset of the anginal pain as a preventive agent, but not after the anginal pain has occurred as caused by the coronary artery constriction and an impairment of coronary blood flow and oxygen delivery to the cardiac musculature has commenced.⁶ As a result of the peripheral vasodilation, amlodipine may precipitate episodes of edema, particularly around the ankles and

lower extremities and is a useful clinical marker for adjustment of the maximum tolerated dose for an individual.⁶

Micronutrient, Antioxidant and Vasorelaxation effects: Pharmacognosy of TCM formulas. TCM formulae derive from a wide variety of plants that are native to their original environments, and exhibit broad variations in their effectiveness in part as a likely reflection of their substrain differences, plant maturity, seasonal differences, and their agricultural environments, especially if transplanted from their original location to a region with different soil complexity and nutritive value to the plant species.^{1-3,7,8} Thus, roots such as Ginseng species although demonstrate some overriding physiologic similarities when consumed, tend to differ in their overall spectrum of pharmacognosy properties when harvested from Asian vs. North American soils. Moreover as soils become depleted of specific nutrients due to erosion, seasonal and environmental variations, inadequate crop rotation or overuse, the final composition of the vegetation may become depleted of the same nutrient or enriched should fertilization of the soils become suitably enhanced as may occur with recent volcanic soils or following fertilizer overuse and abuse.

The broad variety of TCM actions at the organ, tissue or cellular level contribute to the micronutrient content of the specific agents, including the availability of both water soluble (B complex and C) and fat-soluble vitamins (A, D, E and K), which are typically abundant in green leafy plants. In addition, plant sources typically contain hundreds of complex organic molecules and compounds that when consumed, act as antioxidants and reactive oxygen scavengers (ROS entities) that are physiologically active in preventing free-radical induced inflammatory responses and thus help to bring about their nutraceutical and pharmacologic actions and enabling the normal physiologic processes to occur uninhibited or with decreased levels of inhibition. Of interest, more than one quarter of currently available allopathic medications were derived from plant sources including many that have their origins in traditionally used in folk medicine, natural medicine and TCM therapies, and when applied in concert with allopathic medications often provide synergistic improvements in clinical management of hypertension.^{7,8}

Micronutrient and Antioxidant effects: Mango-Ginger tea. The blood pressure lowering effects of mango- ginger tea or mango flesh consumption on blood pressure are unclear but like the TCM effects indicated above are presumed to be related at least in part to the synergism between the micronutrient and antioxidant content of the mango leaves and phenolic constituents of the ginger, in addition to a mild thiazide-like diuretic effect.^{4,7,10} Mango leaves contain a magnesium-complex known as magniferin, a mineral and antioxidant rich constituent.⁶ Mango leaves are routinely harvested from the common evergreen mango tree (*Mangifera indica* L), a member of the Anacardiaceae family, common in many tropical and subtropical environments. Mangos form part of an important tropical fruit crop from the Caribbean, and tropical regions of South and Southeast Asia, where they grow in abundance in part due to the mineral and nutrient rich soils found especially in volcanic soils common to the Caribbean and other tropical regions. In addition to harvesting and distribution of the Mango fruit, the leaves and decidua of the trees have been harvested for their naturally occurring phytotherapeutic potential.

Mango leaves are the potential source of numerous minerals, including nitrogen, potassium, phosphorus, iron, sodium, calcium, magnesium, and vitamins A, B, E, and C.⁸⁻¹⁰ In addition, a major bio-macromolecule protein is also found in mango leaves, thereby adding to the nitrogenous nutrient content of the extracts and decoctions.

Mango leaves and mango tree residuals resulting from tree husbandry activities are nontoxic and can be safely utilized as an alternative source of livestock feeding in developing countries for alleviating potential food shortages for livestock. Extracts of the mango leaves have been utilized for traditional medicines to treat numerous human illnesses including hypertension, diabetes, bronchitis, diarrhea, asthma, kidney, scabies, respiratory problems, syphilis, and urinary disorders.⁶ Because the minerals occur in association with multiple

organic residues, their luminal absorption is greatly improved when compared to non-organic mineral sources.^{7,9} Magnesium is a useful therapeutic agent especially when administered orally as an amino acid chelate- complex form to bring about muscle relaxation for both vascular and uterine smooth is muscle. Magnesium is also a critical mineral for ATP regeneration and actions, where it has found several clinical uses in exercise physiology and other clinical applications.⁹ The effects of ginger appear to provide synergistic actions to those of mango preparations. Ginger root and ginger extracts contain abundant amounts of active antioxidant- promoting constituents, such as phenolic and terpene compounds.^{7,10} The phenolic compounds in dry ginger are mainly gingerols, shogaols, and paradols, while in fresh ginger, gingerols including 6-gingerol, 8-gingerol, and 10-gingerol are the major polyphenols, all of which exhibit antioxidant actions.⁷

In the SWT formulation study, a group of 30 patients (23 female, 7 male) with mild to moderate hypertension (mean BP >141/95, BMI <30) were monitored over a 90-day duration before and after addition of the SWT treatment as outlined previously.⁴ No side effects were reported in the SWT group, but the allopathic control group reported symptoms of dizziness, double vision, and other unpleasant side effects while taking the allopathic regimen.⁴ The study was approved by the USAT Institutional care and use committee.

For the Mango Leaf-ginger tea trial, the patient was a middle-aged Caucasian male, age 65yr. with well controlled Type II diabetes (HbA1c < 6.8), a BMI of 25, and mild to moderate hypertension and no other medically significant disorders. The combination multidrug treatment for hypertension consisted of therapeutic dosages of 200mg of metoprolol succinate (Extended-Release form), 50mg of losartan potassium twice daily, and 5mg of amlodipine was taken at 8AM (or 8AM plus 8 PM daily where twice daily administration was prescribed), and the mango leaf+ginger tea (one serving) plus 6 slices (½ of a medium size fresh mango) were taken daily approximately 12hours later, one hour prior to bedtime. All medications and nutraceutical agents were taken diligently and exactly as prescribed or recommended without exception. Treatment for NIDDM consisted of dietary control, in addition to metformin (1,000mg daily) and glipizide (2.5mg twice daily). Blood pressure monitoring was determined while sitting in a quietly resting state as outlined by Njoloma et al.¹¹ All measures of SBP and DBP in this case study were taken by AAS with an electronic cuff (Health point USA, Blue Ocean Ecom Limited, Hillfoot, Formby Lane, Ormskirk, L39 7HG.) 2 to 3 times daily and recorded as mm of Hg. Data were plotted as the mean ±1 SEM where indicated and represent 4-6 repeated measurements during each week of the study with the Prism graphics program.¹² No adverse effects to the multidrug combination or to the mango leaf+ginger tea preparation were reported by the subject while conducting this case study. This clinical case study trial was approved by the Institutional care and use committee.

Results

The effect of the allopathic regimen and the TCM-SWT regimen on blood pressure are depicted in Figure 1 and indicate that average

SBP and DBP measures before drug administration were in the mild to moderate hypertension range with consistent values greater than 140/90 as reflected in the left panel of Figure 1. Blood pressure improved after administration of the allopathic regimen (center panel) and indicated modest further improvement in both systolic and diastolic parameters when switched to the TCM-SWT formula.

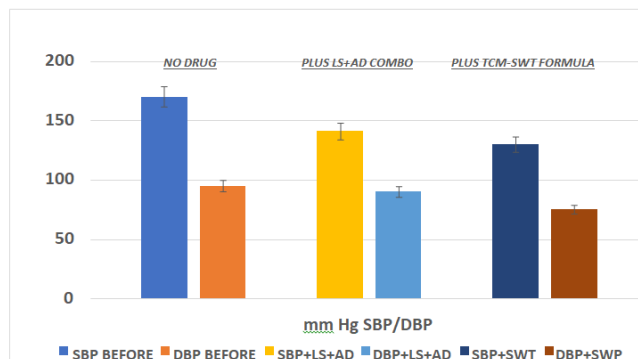


Figure 1 Data are the mean ±1 SEM, N=30. SBP = Systolic BP; DBP = Diastolic BP; All BP measures taken at end of study; LS = losartan; AD = amlodipine, all treatments were for a minimum of 90 days duration. Ref: Chow et al.4 (2021). Data extracted from ref 4.

The effects of the allopathic hypertension treatment before and after 2 and again after 4-6 hours after dosing are depicted in Figure 2 and indicate that allopathic regimen was ineffective in controlling blood pressure parameters after 4 to 6hours post treatment and thus was deemed ineffective in controlling systolic blood pressure throughout the remainder of the day, while diastolic pressure changes although marginal tended to fare more favorably at the 46-hour readings.

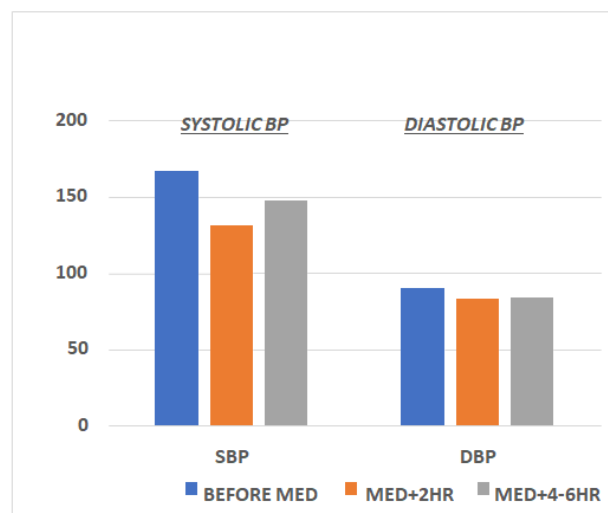


Figure 2 The effect of an allopathic hypertension regimen on blood pressure parameters before and after administration of the multidrug combination. Blood pressures are reported in mmHg and were recorded over a duration of 4 weeks.

The mango leaf-ginger tea combination was added to the allopathic pharmacologic regimen in an attempt to improve the clinical management of chronic mid-grade hypertension (HTN) in a non-insulin dependent (NIDDM) patient with effective glycemic control. Measures of systolic and diastolic blood pressure (SBP and DBP respectively) were obtained for the 4weeks of control monitoring when taking a multidrug pharmacologic treatment consisting of a

combination of the drugs metoprolol succinate, losartan potassium, and amlodipine (MLA regimen) for 6 months or more, followed by 4 weeks of a mango-leaf+ginger tea (MGT) combination. Measures of systolic (SBP) and diastolic BP (DBP) were obtained 6-12 hours after the multidrug regimen and resulted in a 13% decrease in both SBP and DBP after one week, a 17% reduction in both parameters after two weeks, and a 30% reduction at weeks 3 and 4 of the MGT trial. These results indicate that the addition of the Mango leaf+ginger (MGT) natural product regimen when added to the MLA treatment contributed to a normalization of BP and an amelioration of HTN when the MLA regimen alone was incompletely effective due to multi-drug resistance or other factors. The effects of a once daily mango flesh plus mango-ginger tea supplement to the allopathic regimen on blood pressures over a 4-week trial are graphically depicted in Figure 3 and indicate that both SBP and DBP resulted in incomplete control of hypertension (Dark Blue and Orange bars, respectively), with mean values remaining above 140/90 throughout the four weeks of observation. In contrast, upon addition of the MGT supplement to the allopathic regimen, systolic pressures dropped by 13% after one week, 17% after two weeks, and remained stable at approximately 30% below pre-supplement values thereafter (Red Bars).

The decrease in diastolic pressures (Light blue bars) reflected a similar proportionate decrease to that of the systolic pressures and also remained stable with a ~30% reduction at the three- and four-week points. Thus, the MGT regimen was associated with a gradual and lasting normalization of both systolic and diastolic blood pressure parameters that had not been achieved with the allopathic regimen alone. The polynomial trend lines r^2 reflected a value of 1.0, further reinforcing the relative values obtained. It is noteworthy that the measurements depict the values obtained from a single individual, but are entirely consistent with an earlier report of the positive impact on blood pressure measurements when consuming native mango leaf tea in the Caribbean, where mango trees grow in abundance and the mango leaf tea is a commonly consumed beverage for the treatment and management of mild to moderate hypertension.⁴ These results indicate that the addition of the MGT natural product regimen when added to the allopathic drug combination therapy contributed to a normalization of BP and an amelioration of HTN parameters when the MLA regimen alone was incompletely effective due to multi-drug resistance, inadequate dosage, or other factors (Figure 3).

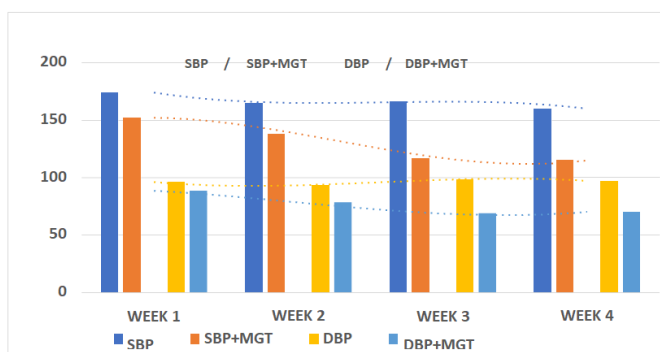


Figure 3 Effect of Mango-Ginger tea supplement on Blood Pressure over 4 weeks of observation. Data are mean of 2-5 replicate measures at each time point. Trend lines $r^2 = 1.0$ (3rd order polynomial).

Discussion

The clinical manifestations of hypertension are often present without exhibiting overt symptoms, particularly during the early stages of the disorder, but the pathophysiologic sequela commence

well before overt symptoms may become evident, resulting in the often-referenced moniker as a ‘silent killer’ of those affected.¹³⁻¹⁶ The prevalence of hypertension ranks among one of the most challenging disorders in global public health concerns especially in patients with the presence of an NIDDM glycemic comorbidity. Hypertension is often poorly controlled or not controlled at all, and impacts the health of approximately one quarter of the adult population despite the ready availability of numerous largely effective pharmacotherapeutic agents in Westernized societies.¹⁴ However, not all patients are managed adequately when taking one or more prescription agents for a variety of factors, and secondly, not all patients may enjoy ready accessibility to the usual assortment of antihypertensive agents due to the combined effects of economic, geopolitical and other factors.¹⁶ For many, the use of Complementary and Alternative Medicines (CAM) including various natural remedies to treat the common disorders and illnesses that may afflict humankind become the first and sometimes the only available line of therapeutic agents for a family member, loved one or member of their community.¹⁷ The practice of Traditional Medicine, which utilizes a wide variety of time proven natural remedies is common in many nations, and is growing in popularity and preference in Western Societies.¹⁻³ Natural therapies have been used successfully in Traditional Chinese Medicine (TCM) as well as in numerous other cultures for thousands of years, and long predate the more recent development of pharmaceuticals over the past decades for the treatment of illness and disease. In a previous report, both TCM and a mango-leaf preparation were found to be effective in treating mild to moderate HTN.⁴

Thus, the purpose of the present paper was to review the effectiveness of a traditional Chinese natural regimen (the TCM regimen containing the above SWT treatment) in a clinical trial, and an herbal remedy consisting of mango flesh equivalent to one half of a mango plus a mango leaf-ginger combination as a tea when added to a traditional multidrug therapeutic regimen for the management of hypertension in an adult male with well-controlled NIDDM but no other significant illnesses. Both complimentary regimens resulted in improvements in blood pressure parameters, and in a sustained

normalization of hypertension. While the mechanisms of action contributed by the Complimentary therapies remains unclear, both represent plant sources rich in multivitamins A,C,D, and K in addition to a myriad of complex organic compounds that contribute antioxidant actions in peripheral tissues, with the expected result of reducing indices of inflammatory action including ROS and others.^{7,8,17} Varying degrees of adiposity as a comorbidity are also often present in hypertensive individuals, and likely serve as an additional contributor of inflammatory cytokines which when left unquenched, may contribute further to the pathophysiologic sequela of hypertension and to complications in its effective management.¹⁷ Regardless of the various mechanisms of action that the complimentary therapies may have contributed to both the TCM and Mango leaf preparations were found to be effective in amelioration of hypertensive parameters, and likely to improved healthful outcomes if continued over a prolonged duration.^{4,7,8}

Hypertension is a common condition that impacts approximately one quarter of the adult population of Westernized Society, and when left untreated, can serious and often life-threatening injury to the brain, heart, blood vessels, kidneys and other organs and tissues.¹³⁻¹⁶ Hypertension is often referred to as a ‘silent killer’ as during the early stages of disease progression the individual may remain asymptomatic and may not recognize the subtle nature of early symptoms of an impending hypertensive or cardiovascular disorder. Numerous factors can contribute to the gradual progression of hypertension, including

diet, exercise, excess weight gain, lifestyle practices, smoking, excessive alcohol consumption, comorbidities, and likely genetic predisposition.

Monitoring the above factors within moderation alone can be partially if not wholly preventive in most individuals, and the strategic incorporation of a medication and therapeutic regimen tailored to the individual may slow or prevent the majority of further progression of hypertensive related disorders. For reasons that often remain unclear, medications as monotherapy or combination therapy of available treatment agents may not always bring about the desired return toward a normotensive state, thereby requiring the incorporation of adjustments in diet and lifestyle activities. These typically include consuming a diet that is low in fat, salt, and caloric content, developing a healthy weight, especially the lowering of visceral adipose tissue, exercising at least 30 minutes most days, not smoking, and using alcoholic beverages in moderation in addition to careful monitoring of the progression of comorbidities when present.¹³⁻¹⁶

The consumption of mango leaf tea is a common practice in certain parts of the world, including the Caribbean where nutrient rich volcanic soils and a tropical environment are common and the presence of fruiting mango trees are often abundant.⁴ The tea is prepared fresh by crushing a few fresh or dried mango leaves in a liter or so of water, steeping for about 15 minutes or just left overnight in room temperature water in order to extract the water soluble elements and is deemed sufficient to extract the essential principles from the leaves. The tea may be consumed as soon after preparation as is desired and is usually consumed while freshly prepared and still warm and pleasant to the taste.^{4,18} While natural or artificial sweeteners such as natural honey may be added to taste, they usually are not required. The mango-ginger tea used in the present case study is a useful modification of the traditional Caribbean mango leaf tea in that the Ginger provides additional antioxidant properties that can address potentially malevolent issues of inflammation in peripheral tissues, especially when inflammation-prone visceral fat stores are increased, and thus complement the nutraceutical impact of the mango leaf extract provided by the addition of ginger to the tea. By incorporating the tea into an allopathic pharmaceutical multidrug regimen, the tea can add effectively additional vital phytochemically-mediated elements to the overall mechanisms of action that the base regimen may not have incorporated or recognized.

The home preparation of the SWT formula is similar to the mango leaf preparation in that a tea or an aqueous decoction is prepared with warm or room temperature water.⁴ In studies of the efficacy of natural products and losartan, Lai et al.¹² evaluated a traditional Chinese natural product remedy in a large cohort of patients (over 1000 patients in all) with mild to moderate hypertension, who were taking either the traditional Chinese Medicine (TCM) or the losartan regimen and found the outcomes to be equivalent to those of a daily 50mg dosage of losartan in controlling both systolic and diastolic pressure.¹⁹ In another study by conducted by Chow et al.²⁰ the authors also reported a similar outcome success when comparing a traditional ancient TCM regimen (the THSWT or SWT described above) to allopathic medications in patients with mild to moderate hypertension, and Tulp et al. reported a case study that demonstrated the efficacy of mango leaf tea as monotherapy in controlling markers of mild to moderate hypertension in Montserrat in the absence of availability allopathic medications, and where the consumption of locally-prepared mango leaf tea is common.^{4,20}

In the present case studies reviewed above, it became apparent that the single daily dosage of the allopathic medication combination

was inadequate to provide effective 24-hr control of blood pressure measurements, with the effectiveness of the regimen beginning to wane within 4 to 6 hours after morning drug administration, suggestive of early drug clearance, multidrug resistance, or some combination of the two factors. While the multidrug regimen provided effective systolic blood pressure control in the early hours following administration, diastolic blood pressures reflective of peripheral vascular resistance, were only partially normalized during the first 2 hours, but also returned to pretreatment levels later in the day.

Thus, the multidrug regimen when taken alone as typically prescribed was not completely successful in effective clinical management of hypertension throughout the day and evening as the therapeutic half-life of the dosages administered appeared to have been inadequate for an optimal outcome to have occurred. Were the dosages adjusted to higher levels or if additional antihypertensive agents or repeat dosages were to be added to the regimen, the potential for adverse side effects of the multidrug combination would also likely have necessarily increased. Thus, the decision to incorporate modest quantities of a naturally occurring nutraceutical agent with no known side effects when consumed as directed to the partially effective multidrug regimen was deemed a reasonable clinical course of action in an attempt to improve hypertensive parameters over a longer duration. The mango leaf-ginger combination was selected due to the antioxidant and micronutrient properties of the tea, which would then incorporate yet an additional mechanism of action to the multidrug combination therapy in addition to the reported efficacy of the tea as a monotherapy in managing hypertension of mild to moderate severity. While the pharmacologic agents each typically report a single mechanism of action, the mango leaf+ginger tea contains a plethora of antioxidant and micronutrient constituents which when combined with the allopathic agents, was observed to extend the mechanism and effective duration of action in such manner that vascular elasticity and peripheral resistance appears to have become improved, thereby enhancing the effectiveness of the allopathic agents. The ginger component in combination with the micronutrients has also been reported to increase the process of angiogenesis, thereby further enhancing the clinical effectiveness of the nutraceutical addition to the antihypertension regimen and suggest that additional trials of a longer duration may be helpful and perhaps may help lead to a further explanation of the complex mechanisms of action implicated in the vascular responses and in the pathophysiologic contributors to hypertension.

Summary and conclusions

The results of this clinical case study review indicate that the addition of a long-traditional TCM remedy (the SWT formula) and a commonly available Mango Leaf+ Ginger tea plus mango fruit flesh to a multiagent allopathic regimen for the management of moderate hypertension was effective in improving the clinical outcome of the hypertension parameters after a loading time duration of 2 to weeks of observation for both complimentary treatments. The blood parameters demonstrated moderate improvement beginning within one week of observation, additional improvement at the 2-week marker, and which resulted in sustained normalization of both systolic and diastolic blood pressures after 3 and 4 weeks of observation. Although the parameters of NIDDM were not specifically included in the study they remained in adequate control throughout the study. The physiologic basis for the nutraceutical-mediated improvements is unclear and could not be determined from the study but are presumed to be due at least in part to the broad phytochemical content of the SWT, the mango leaf and ginger components, which are well established to reduce excess ROS

activity and to augment antioxidant reducing activity in peripheral tissues while enabling improvements in physiologic parameters over time. The basis for the incomplete clinical management of hypertension with the aggressive multidrug regimen undertaken in the two studies remain unclear but may be linked at least in part to prior vascular pathophysiologic processes which may have occurred secondary to the longstanding NIDDM which was also present in some patients. Because NIDDM and obesity are established risk factors for hypertension, even when adequate plasma glucose control measures have been incorporated into a patient's treatment plan, the NIDDM likely contributed at least in part to the clinical outcome in this individual.^{2,15} Like hypertension, symptoms of NIDDM contribute to peripheral vascular injury and also may be unrecognized during the early stages of development of the disorder and thus may result in additional complications in later attempts for clinical management of pathophysiologic NIDDM sequela. The Mango leaf – ginger tea provided magniferin, antioxidants, and numerous micronutrients and phytochemicals that are conducive to improving parameters human health, while the exact chemical composition of the SWT formula is unclear but owing to its plant-based origins likely contains similarity in at least some of the antioxidant-enhanced constituents.

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Conflicts of interest

We declare there are no conflicts of interest.

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