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Sweet basil leaves as adjunct therapy for stage 1 and 2 hypertension: a pilot clinical trial

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ABSTRACT: *Ocimum basilicum* L. (Sweet Basil) is a medicinal herb used in traditional Indian and Chinese medicine to treat a variety of disease conditions including hypertension, and has well established antihypertensive effects among renovascular hypertensive rats. The aim of this study was to evaluate the antihypertensive effects of *O. basilicum* as adjunct in the management of stage 1 and 2 hypertensive patients. A double blind-randomized controlled trial was performed, with participants (n=24) randomized into a control and treatment group. Participants randomized into the control group (n=12) were given their prescribed antihypertensive medication plus placebo while those in the treatment group (n=12) were given their antihypertensive medication plus *Ocimum basilicum* L. capsules containing 128 mg of dried, powderized leaves once a day. Participants' blood pressure (BP) was measured at baseline, 1 week, and 2 weeks of drug administration and the Mean Arterial Pressure (MAP) calculated. Results showed that systolic and diastolic BP in the treatment group measured from baseline, one and two weeks of drug administration are significantly different, whereas the control group had insignificant findings. Furthermore, the MAP in the control group (105.25±9.52 mm/Hg, 104.08±8.45 mm/Hg and 104.47±8.85 mmHg) were comparable while that in the treatment group (106.47±6.65 mm/Hg,100.89±9.99 mm/Hg, and 97.14±9.96 mm/Hg) showed significant lowering (p=<0.0001) over time by Repeated Measures-Anova with Bonferroni's post-hoc test. The significant findings in this study support the antihypertensive action of *Ocimum basilicum* L. among humans which warrant further exploration.

Keywords: *Ocimum basilicum* L.; Sweet Basil; Basil; Hypertension; Mean Arterial Pressure; Adjunct Therapy; Anti-Hypertensive drugs; Randomized Controlled Trial; Pilot study.

1. INTRODUCTION

Hypertension is one of the most pervasive chronic conditions that afflicts approximately 30% of adults, with a steadily increasing rate. Its complications include coronary heart disease, stroke, peripheral vascular disease, visual impairment and renal failure. In the presence of any of these concomitant disease or comorbidity, hypertension can serve as a confounding factor which can increase morbidity and mortality [1]. The current standard of care in the pharmacologic management of hypertension according to American Heart

Association (AHA) 2020 guidelines includes a Angiotensin-II converting enzyme Inhibitors (ACE-I)/ Angiotensin Receptor Blockers (ARB), Dihydropyridine Calcium Channel Blockers (CCB) and/or a Diuretic (Thiazides/Potassium Sparing) depending on the class of hypertension diagnosed, and associated comorbidities [2]. To date, no herbal-based remedy has yet been approved as efficacious among humans. However, WHO reported that about 80% of the population, especially those of developing countries still rely on traditional medicine for their primary health care needs [3]. Herbal based medications are also theoretically much cheaper and when of suitable quality, safer considering their widespread availability and use by indigenous populations [4].

Studies on *Ocimum basilicum* L. (Sweet Basil) have shown anti-hypertensive, hepatoprotective, anti-diabetic, hypolipidemic, analgesic, anti-inflammatory, anti-microbial, anti-oxidant, anti-ulcerogenic and larvicidal activities of the herb [5]. The strong clove scent of *O. basilicum* is derived from its compound, eugenol, a vanilloid molecule. The anti-hypertensive effect of Basil could be attributed to several of its constituents including eugenol [6-9] and linalool [10-12], postulated to have vascular vasodilatory actions. The anti-hypertensive properties of *O. basilicum* have been demonstrated on renovascular hypertensive rats in prior studies [13, 14]. Since basil is normally eaten, toxicity is not a problem. This study aimed to use a locally available medicinal herb, *O. basilicum*, as an adjunct therapy to manage blood pressures of stage 1 and stage 2 hypertensive patients. This clinical trial is the first of its kind which determines the efficacy of basil among human subjects.

2. MATERIALS AND METHODS

This research study was a double-blinded randomized controlled pilot clinical trial. Volunteer participants who fulfilled the inclusion/exclusion criteria were recruited from a village in Davao City, Philippines. A volunteer was considered if he/she was above the age of 18, diagnosed with stage 1 or stage 2 hypertension as dictated by JNC7 criteria [15], and on anti-hypertensive maintenance medications. Exclusion criteria included patients who were medically unstable, allergic to basil, suffering from any infection or communicable disease, and participants on any other supplements or treatments which could affect blood pressure.

The study followed a simple randomization method (fishbowl technique) to allot 24 hypertensive volunteer participants into two groups, the control group (n=12) and the treatment group (n=12). Participants in the control group were given their prescribed antihypertensive medications plus a placebo capsule while the treatment group received their prescribed medications plus an *O. basilicum* capsule daily for 2 weeks. Blood pressure of the participants were recorded at baseline, after 1 week, and at the end of the 2nd week. The blood pressure was obtained by using an aneroid sphygmomanometer. Gauge accuracy was checked visually by making sure that the needle rests at 0 when the unit was fully deflated. The average value of the 3 blood pressure recordings was noted.

The preparation of the capsule containing basil was as follows: commercially available sweet basil leaves were purchased. The samples were cleaned of earthy material, rinsed with distilled water and prepared for cabinet drying. Services of Food Processing and Innovation Center, Philippine Women's College, Davao City were utilized to assure food grade processing of the leaves, where after 6 hours of drying at 40°C, the dehydrated leaves were sealed and brought to Davao Medical School Foundation for encapsulation.

Freeze drying of herbal products is used for pharmaceutical purpose as it is believed to retain the characteristics of the bioactive components [16]. Owing to the high cost of freeze drying, oven drying was the most practical option for the research team. A study on dried medicinal herb states that cabinet drying retained

the nutritional components of the sample efficiently. Supportive scientific facts on eugenol's chemical properties assured its property retention even at 40°C [17].

The dosage used in this study was based on the study of Umar, 2012 [13]. A medium dose of 200mg/kg was chosen. This effective dose in animals was converted to human effective dose using the formula developed by Nair, 2016 [18]. Considering the average weight of humans to be 60 kg, the 200 mg/kg animal effective dosage (in rats) was converted to 32mg/kg human effective dose. Human Effective Dose (HED) was calculated as, HED (mg/kg) = Animal dose (in mg/kg) x Animal Km/Human Km. Data obtained from FDA guidelines show that Rat Km is 6, whereas Human Km is 37. Hence, HED (mg/kg) = 200*6/37= 32 mg/kg. In the prior study on hypertensive rats, a pure extract of Ocimum Basilicum leaves was used, whereas our study utilized powdered dried leaves instead.

The effective human dose of 1920 mg (32 mg/kg for a 60 kg adult) of fresh *Ocimum basilicum* L. leaves were crushed and upon drying and dehydrating, yielded 128 mg of dried leaves per capsule. Placebo capsule on the other hand was prepared by purchasing commercially available starch, which was capsulated in Davao Medical School Foundation Research Center, similar to the basil capsule. The appearance of the basil and placebo capsules were made similar as both were red in color, non-translucent and of the same size and shape.

As a double blinded study, the participants and the research team members providing the participants with the capsule were unaware of the contents of the capsule provided (whether basil or placebo), with the exception of the study team personnel handling data compilation and computation. The data collected included systolic and diastolic blood pressure, from which Mean Arterial Pressure (MAP) was calculated. Mean Arterial Pressure is calculated as the sum of 1/3*systolic BP + 2/3*diastolic BP. All data were stored on a secured, encrypted server and were accessible only to study team personnel. Statistical analysis was done using Repeated Measures Analysis of Variance (with 95% confidence interval) with Bonferroni's post-hoc test which determined where the significant differences lie among the groups through time.

3. RESULTS

Twenty four (24) adult hypertensive volunteers were randomly assigned to to the control (n=12), and the treatment (n=12) group. No attrition was reported, and results of all the participants were appropriately analysed. Table 1 shows the demographic and baseline characteristics of the participants in the study. Comparison between the control and treatment group showed no significant difference in all parameters measured. Thus, the two groups were comparable at the beginning of the study.

Table 1. Comparison of the baseline characteristics among the participants in the control and treatment groups analyzed using independent *t*-test for continuous and Chi-square test for categorical variables.

Variable		Control group	Treatment group	*p*-value
Age (Mean ± SD)		50.92 ± 20.44	55.92 ± 10.54	0.459
Sex (Freq/%)	Male	7 (29%)	3 (13%)	0.098
	Female	5 (21%)	9 (37%)	
Baseline BP (Mean ± SD)	Systolic	140.42 ± 19.50	139.58 ± 8.69	0.894
	Diastolic	87.67 ± 6.47	89.92 ± 7.55	0.441
Baseline MAP (Mean ± SD)		105.30 ± 9.52	107.10 ± 6.674	0.590

*Significant *p*-value at 0.05 level.

Data on the blood pressure monitoring showed that the mean systolic and diastolic blood pressures of the participants in both the control and treatment groups had a general downward trend over time (Table 2). However when this trend was analyzed through Repeated Measures ANOVA, no significant difference was found in the control group from baseline, 1 week and 2 weeks of drug administration. On the other hand, the mean systolic and diastolic blood presures of the participants in the treatment group were significantly different over time (Table 2). This means that the addition of basil capsule in the treatment group resulted to significant additional lowering of the blood pressure among the participants over time.

A similar trend was noted in the MAP with significant lowering over time in the treatment group and no significant difference in the control group (Table 2).

Table 2. Comparison of the mean systolic, diastolic and MAP of the participants in the control and treatment group over time analysed using repeated measures ANOVA with Bonferroni post-hoc test.

Variable	Group	Time	Mean ± SD	*p*-value
Systolic	Control	Baseline	140.42 ± 19.50	0.105
		After 1 week	137.58 ± 16.78	
		After 2 weeks	136.83 ± 17.01	
	Treatment	Baseline	139.58 ± 8.69[b,c]	< 0.0001*
		After 1 week	133.00 ± 12.63[a,c]	
		After 2 weeks	127.58 ± 13.73[a,b]	
Diastolic	Control	Baseline	87.67 ± 6.47	0.457
		After 1 week	87.33 ± 6.51	
		After 2 weeks	86.25 ± 4.73	
	Treatment	Baseline	89.92 ± 8.69[b,c]	0.001*
		After 1 week	84.83 ± 10.10[a]	
		After 2 weeks	81.92 ± 9.39[a]	
MAP	Control	Baseline	105.21 ± 9.51	0.137
		After 1 week	104.05 ± 8.46	
		After 2 weeks	103.08 ± 7.75	
	Treatment	Baseline	106.43 ± 6.66[b,c]	< 0.0001*
		After 1 week	100.86 ± 10.00[a]	
		After 2 weeks	97.10 ± 9.95[a]	

*Significant *p*-value at 0.05 level. a. Significantly different to Baseline. b. Significantly different to after 1 week. c. Significantly different to after 2 weeks.

Bonferroni's post-hoc test further revealed that the significant difference in the systolic pressure was noted between 1 and 2 weeks while that in the diastolic pressure was noted between baseline and 1 week but no significant lowering was noted between 1 and 2 weeks. This could mean that for the systolic pressure, basil's most significant lowering effect was noted on the 2nd week of drug administration. On the other hand, the effect of basil for the diastolic pressure was noted earlier after the 1st week and levelled off towards the 2nd week. This same observation was noted for the MAP. Overall, the results showed that the addition of basil capsule (128 mg/capsule) on the maintenance antihypertensive drugs prescribed to the participants caused further lowering of blood pressure starting at 1 week and continued on up to the 2nd week of basil administration. No unintended or adverse effects were noted.

4. DISCUSSION

Ocimum basilicum L., Sweet Basil has a variety of proven and postulated benefits, of which the anti-hypertensive effect was demonstrated in humans in this pilot study. Through the centuries, basil was cultivated for culinary and medicinal purposes in many countries, which created a great diversity of species within the *Ocimum* genus: the genus *Ocimum* comprises more than 150 species and is considered as one of the largest genera of the Lamiaceae family [19].

Major constituents of the essential oil extracted from *Ocimum basilicum* varies by region, possibly varying with season, cultivation and subspecies. The aroma of each subspecies of *O. basilicum* is dependent on its major chemical constituents including monoterpenes and phenylpropanoids. In a study on 270 sweet basil accessions, the main components in the essential oils found were linalool (max. 71%), methyl chavicol (max. 92%), citral (max. 80%) and 1,8 cineole (max. 25%) as well as camphor (max. 63%), thymol (max. 35%), (E)-methyl cinnamate (max. 77%), eugenol (max. 80%), methyleugenol (max. 79%), methyl isoeugenol (max. 36%) and elemicin (max. 47%) [20].

A European study published in 2020 revealed that the major components of *Ocimum basilicum* L. essential oil include linalool (18.0–68.0%), methyl chavicol (0.0–57.3%), geraniol (0.0–16.5%), 1,8-cineole (1.4–15.1%), p-allylanisole (0.2–13.8%), eugenol (0.0–12.32%), limonene (0.2–10.4%) [21]. Unfortunately, constituents of the essential oil of *O. basilicum* in the Philippines is not demonstrated in any prior studies. This could be a good topic for future studies.

Among the major constituents of *O. basilicum* mentioned in literatures, several compounds may contribute to the blood pressure lowering among the participants treated with the basil capsules in this study. These are eugenol [6-9], linalool [10-12], geraniol [22, 23] and limonene [24, 25].

Eugenol is theorized to stimulate TRPV channels leading to large conductance potassium channel (BKCa) activation and smooth muscle hyperpolarization, leading to vasodilation [7, 8]. Vasodilation can decrease the peripheral vascular resistance which can decrease blood pressure, since blood pressure in a product of cardiac output and peripheral resistance [9]. Any factor that can decreases peripheral resistance will also decrease blood pressure.

Linalool is a terpene alcohol present in large quantities in *O. basilicum*, especially in the European varieties. Linalool demonstrated a dose-dependent vasodilatory effect in hypertensive rats, and elicits these effects by activation of guanylyl cyclase and K^+ channels in vasculature of the rats, and increased levels of anti-inflammatory cytokine IL-10 [10-12].

Geraniol, present in minor quantities was found to alleviate complications of diabetes in rats, especially improving vascular reactivity through a calcium channel blocking effect [22, 23]. Limonene, present in minor quantities in *O. basilicum* is considered as a lipid lowering agent with antioxidant properties, and may also have blood pressure lowering qualities [24, 25]. Hence, these preclinical studies have demonstrated that many components of *O. basilicum* possess anti-hypertensive effect, especially eugenol and linalool present in relatively high quantities in varieties of *Ocimum basilicum* L.

Basil can be grown easily in anyone's backyard and the fact that it's considered food, people can be assured of its safety. Oven drying at 40ºC can be done in an ordinary household oven so the usefulness of basil can easily be utilized by the community. The results of this study should encourage other researchers to do a follow up study in a bigger population. Dosage range can also be explored. Regardless of this being a pilot study with a small sample size, the results are nevertheless encouraging. Thus, future researches are warranted which can validate the results of this study in a bigger population.

5. CONCLUSION

This pilot clinical trial demonstrated a significant anti-hypertensive effect of *Ocimum basilicum* L. (Sweet Basil) dried leaves at 128 mg/capsule, one capsule a day as adjunct to maintenance antihypertensive medication that led to further lowering of the blood pressure among Stage 1 and 2 hypertensive patients. Further studies are warranted.

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