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CLINICAL INVESTIGATIONS

A defined, plant-based diet utilized in an outpatient cardiovascular clinic effectively treats hypercholesterolemia and hypertension and reduces medications

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Background: Cardiovascular disease (CVD) is a major economic burden in the United States. CVD risk factors, particularly hypertension and hypercholesterolemia, are typically treated with drug therapy. Five-year efficacy of such drugs to prevent CVD is estimated to be 5%. Plant-based diets have emerged as effective mitigators of these risk factors.

Hypothesis: The implementation of a defined, plant-based diet for 4 weeks in an outpatient clinical setting may mitigate CVD risk factors and reduce patient drug burden.

Methods: Participants consumed a plant-based diet consisting of foods prepared in a defined method in accordance with a food-classification system. Participants consumed raw fruits, vegetables, seeds, and avocado. All animal products were excluded from the diet. Participant anthropometric and hemodynamic data were obtained weekly for 4 weeks. Laboratory biomarkers were collected at baseline and at 4 weeks. Medication needs were assessed weekly. Data were analyzed using paired-samples *t* tests and 1-way repeated-measures ANOVA.

Results: Significant reductions were observed for systolic (−16.6 mmHg) and diastolic (−9.1 mmHg) blood pressure ($P < 0.0005$), serum lipids ($P \leq 0.008$), and total medication usage ($P < 0.0005$). Other CVD risk factors, including weight ($P < 0.0005$), waist circumference ($P < 0.0005$), heart rate ($P = 0.018$), insulin ($P < 0.0005$), glycated hemoglobin ($P = 0.002$), and high-sensitivity C-reactive protein ($P = 0.001$) were also reduced.

Conclusion: A defined, plant-based diet can be used as an effective therapeutic strategy in the clinical setting to mitigate cardiovascular risk factors and reduce patient drug burden.

KEYWORDS

Biomarkers, General Clinical Cardiology/Adult, Hypertension, Preventive Cardiology, Vegetarian Diet

1 | INTRODUCTION

Cardiovascular disease (CVD) is a major economic burden to the United States. Currently, 17% of all healthcare expenditures go toward CVD care.[1] Projections are expected to rise, as 40.5% of the US population may have some form of CVD by 2030, leading to a near tripling in medical care costs, from $273 billion to $818 billion. CVD has been the leading cause of death in the United States since 1950.[2] The standard of clinical care in the primary prevention of CVD is to reduce CVD risk factors, particularly through lipid-lowering and antihypertensive drug therapy.[3] It has been estimated that nearly 40% of the population has high serum low-density lipoprotein cholesterol (LDL-C).[4] In addition, approximately one-third of individuals age 40 to 59 years are estimated to be hypertensive.[5] Of those with hypertension (HTN), 76% are on medications to reduce blood pressure, but only 52% achieve blood-pressure control. The highest drug prices in the world are found within the United States. On average, per capita spending on prescription drugs in the United States is $858, compared with an average of $400 in 19 other industrialized countries.[6]

Patients' opinion of the efficacy of drug therapy in CVD prevention is often inflated multifold.[7,8] It has been estimated that high-risk

patients have a < 5% chance of benefiting from cardioprotective drugs within the next 5 years. Moreover, most patients wish to take drugs at a benefit threshold of ≥20% over 5 years.[9] Thus, if patients were aware of the actual benefit of cardioprotective drugs, many patients may not be willing to take such medications.

Based on growing evidence,[10–15] it has been recommended that physicians encourage patients to consume plant-based diets.[16] The aim of this investigation was to evaluate the effectiveness of a defined, plant-based diet as an adjunct to or replacement of prescription drugs in the treatment of hypercholesterolemia and HTN in an outpatient clinical setting.

2 | METHODS

2.1 | Study population

All subjects were registered new patients of a cardiovascular center. The study intervention was carried out in an outpatient clinical setting. All participants provided written informed consent after the study protocol and procedure had been fully explained. The study was approved by the Texas Woman's University Institutional Review Board.

Baseline characteristics of the patients are shown in Table 1. All participants were age 32 to 69 years with HTN, elevated LDL-C, and excess body weight. HTN was defined as systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg. Elevated LDL-C was considered to be a serum LDL-C concentration ≥ 100 mg/dL, and excess body weight was defined as a body mass index ≥25 kg/m^2.

Exclusion criteria included current tobacco use, current drug abuse, excessive alcohol use (defined as >2 glasses of wine or alcohol equivalent per day for men or >1 glass of wine or alcohol equivalent for women), a current cancer diagnosis, an ongoing clinically defined infection, a mental disability that would prevent the participant from following the study protocol, an estimated glomerular filtration rate < 60 mg/dL, current pregnancy or lactation, a hospitalization within the past 6 months, and previous exposure to the nutrition program.

2.2 | Screening

Eligibility was determined through initial screening of participants who expressed interest in participating in the intervention. Demographics, lifestyle habits, anthropometrics, and hemodynamics were used to determine the eligibility of participation for each subject. A trained medical assistant measured blood pressure, heart rate, and body weight. Medical history and lifestyle habits were obtained by the medical assistant and/or nurse practitioner. Fasting blood was collected by a licensed phlebotomist. The clinical care of all patients was overseen by a board-certified cardiologist.

2.3 | Weekly visits

After subjects were screened for study inclusion, follow-up appointments were arranged for study enrollment. Participants were instructed to attend 4 follow-up weekly office visits in addition to a baseline assessment. Baseline weight, blood pressure, heart rate,

TABLE 1 Baseline patient demographics and clinical diagnoses

	Participants, n = 31
Mean age, y	53.4 (32–69)
Sex	
M	10 (33)
F	21 (67)
Race/ethnicity	
African American	25 (80)
Hispanic	3 (10)
White	3 (10)
BMI, kg/m^2	37.5 ± 8.3
25–29.9 (overweight)	6 (19)
30–34.9 (obese class 1)	6 (19)
35–39.9 (obese class 2)	10 (33)
≥40	9 (29)
Current diagnoses	
CAD	10 (33)
T2DM	8 (27)
Arthritis	7 (23)
Prediabetes	5 (17)
Medications, n	
BP medications, total	49
ACEI	5
ARB	11
Central antiadrenergic	1
Cardioselective (β1)-blocker	6
Noncardioselective (β1)-blocker	2
CCB	9
Potassium-sparing diuretic	1
Thiazide diuretic	14
Other prescription drugs, total	33
Biguanide	2
Sulfonylurea	3
Dipeptidylpeptidase-4 inhibitor	1
Insulin	2
NSAID	1
Biologic immune suppressant	1
Statin	2
Bronchodilator/steroid inhaler	5
Thyroid drugs	3
Xanthine oxidase inhibitor	2
PPI	1
Antiplatelet	1
Antianginal	2
Digitalis glycoside	1
Vasodilator	1
Other	5
Total medications	82

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BMI, body mass index; BP, blood pressure; CAD, coronary artery disease; CCB, calcium channel blocker; F, female; M, male; NSAID, nonsteroidal anti-inflammatory drug; PPI, proton pump inhibitor; SD, standard deviation; T2DM, type 2 diabetes mellitus. Unless otherwise noted, data are presented as n (%) or mean ± SD (range).

waist circumference, medications, and biochemical indicators were documented. A baseline 24-hour dietary recall was conducted by a trained nutritionist with the utilization of food models to verify portion sizes of foods and beverages consumed. Nutrient intake was analyzed by the Nutrition Data System for Research software, version 2016 (University of Minnesota, Minneapolis).

Follow-up visits (weeks 1–4) consisted of obtaining weight, blood pressure, heart rate, and waist circumference. Medications were assessed and adjusted as needed by the medical doctor or nurse practitioner during the follow-up visits. The final visit (week 4) consisted of a second 24-hour dietary recall and a second collection of fasting blood to assess biochemical measures.

2.4 | Medications

Medications were documented following the conclusion of each office visit. All medications listed at baseline were chronic stable medications (>3 months), except for medications changed during the baseline office visit as outlined in the protocol below. All other medication changes were documented in the medication tracking of this study. No lipid-lowering medications were added at the onset or during the study. The medication needs-assessment protocol is as follows:

- Baseline: All nonessential medications and supplements were discontinued. Additionally, diuretics were discontinued in patients who were clinically euvolemic. Insulin, sulfonylureas, and other potential glucose-lowering medications were either removed or the dosage was decreased in patients whose glucose levels were routinely below 250 mg/dL. All baseline medications are indicated in Table 1.
- Week 1 follow-up: If a patient's blood pressure was low and the patient had symptoms of dizziness or fatigue associated with low blood pressure, then blood pressure medications were decreased by 25% to 50%. Other medications were reviewed with consideration of removal based on patient needs (eg, hypoglycemics).
- Week 2 follow-up: The patients' clinical response to the diet was reevaluated and medication adjustments were made according to their clinical response. Medications primarily prescribed for symptom management were assessed (eg, sleep, allergies, mood disorders, pain) and discontinued if necessary.
- Weeks 3 and 4 follow-up: Based on the patients' clinical response to the dietary intervention, changes were made to the medications as needed for the remainder of the intervention.

2.5 | Dietary protocol

Participants were instructed to follow a defined plant-based dietary intervention for 4 weeks. A food classification system using a scale of 0 to 10 was devised to create a simple, reproducible way of prescribing a nutritional regimen to patients in the clinical setting (Table 2). Participants were instructed to consume foods within this food classification system. Food levels 0 through 4B were permitted, whereas all other food levels were excluded. Briefly, food levels 0 through 4B exclude all animal products, with the exception of honey. Cooked foods, free oils, soda, alcohol, and coffee were also excluded. Emphasized were raw fruits and vegetables, with avocado and raw seeds

TABLE 2 The food classification system

Food Level	Description
0	Liquids including water, tea, unpasteurized fruit and vegetable juices, and blended fruit and vegetable smoothies. These foods would be consumed raw, except for tea, which can be steeped in hot water.
1	Raw fruits and vegetables with a low glycemic index (<56)
2	Raw fruits and vegetables with a medium to low GI (56–70)
3	Raw fruits and vegetables with a high GI (>70)
4A	Plant foods that are raw with a high fat content (≥20% of caloric content from fat), such as raw seeds and avocados
4B	Plant foods that are dehydrated to temperatures ≤160°F
4C	Plant foods that are dried, dehydrated, or warmed (dry-heat cooking) at 160°F–175°F, or steamed or boiled for a short duration (steaming, <4 min; boiling, <10 min). Includes lightly steamed, soaked, sprouted, dehydrated, or warmed fruits, vegetables, legumes or beans, and grains. Heated foods with >20% of calories from fat are excluded.
5	Foods that are warmed, dried, or dehydrated at 175°F to 200°F, and steamed or boiled for a medium duration (steaming, 4–10 min; boiling, 10–45 min). Typical foods include greens, beans and legumes, and starches, including grains, bean or mixed-vegetable soups, and other fruit and vegetables boiled for up to 45 min or oven-warmed (at 155°F–200°F). Heated foods with >20% of calories from fat are excluded.
6	Foods that are baked, warmed, dried, or dehydrated at >200°F, or steamed or boiled for a long duration (steaming, >10 min; boiling, >45 min). Heated foods with >20% of calories from fat are excluded.
7	Fish with low mercury content lightly steamed or poached for ≤8 min. Processed plant foods with preservatives or additives, free oils, and heated foods with >20% calories from fat are included.
8	Same as level 7, except also includes wild-game meats, low-mercury fish lightly steamed or poached for >8 min, and plant-based foods that are grilled or heavily processed. May also include carbohydrates with white flour or white rice, or natural foods that have been stripped of their natural components.
9	Animal-based foods that include domestically raised animals (excluding beef and pork) and plant-based foods that are sautéed, stir-fried, medium-fried or deep-fried in oil. Other animal-based foods include all other types of fish. May also include foods containing dairy products.
10	All other types of animal-based foods, and plant-based foods prepared in any way. May include processed foods of any kind.

Abbreviations: F, Fahrenheit; GI, glycemic index. Food classification levels 0 through 4B were permitted for consumption during the dietary intervention; levels >4B were excluded from the intervention. Sodium consumption was low, although the food provided to patients contained small amounts of sea salt.

provided as condiments. All meals and snacks were provided at no cost to the participants for the full duration of the 4-week intervention. Vitamin, herbal, and mineral supplements were to be discontinued unless otherwise clinically indicated. Participants were not advised to alter their exercise habits, nor were exercise habits monitored.

Participants were free to consume foods outside of what was provided, as long as the foods fell within food levels 0 through 4B. No caloric targets were prescribed, nor were any macronutrient restrictions advocated; participants were free to consume food ad libitum. Participants were also instructed to track dietary adherence with a daily adherence-assessment tool. Participants indicated in writing each day whether they were "100% on the diet" or "ate anything off of the diet." The number "1" was assigned to an adherent day, and "0" was assigned to a nonadherent day. Scores after 4 weeks could therefore range from 0 to 28 points for each participant. Evaluation of the adherence-assessment tool was conducted during each weekly follow-up visit by a trained nutritionist.

2.6 | Biochemical measures

After a 12-hour fast during the baseline and final office visits, the following serum biomarkers were obtained: total cholesterol, LDL-C, high-density lipoprotein cholesterol, triglycerides, insulin, glucose, glycated hemoglobin (HbA_{1c}), and high-sensitivity C-reactive protein (hs-CRP). These specific biomarkers of interest were analyzed by either True Health Diagnostics (Frisco, TX) or Singulex (Alameda, CA), depending on the subject's insurance. The same company that analyzed the baseline laboratory tests for a participant was used for the follow-up testing to ensure assay consistency.

Serum lipids were measured by enzymatic colorimetric assay, and insulin was measured by a no-competitive sandwich-type enzyme-linked immunosorbent assay with electrochemical detection for both True Health Diagnostics and Singulex. Glucose was measured by an enzymatic reference method with hexokinase using colorimetric detection, and hs-CRP was measured by a particle-enhanced immunoturbidometric assay for both Singulex and True Health Diagnostics. HbA_{1c} was measured by a turbidometric inhibition immunoassay for Singulex. Boronate affinity chromatography was used by True Health Diagnostics for HbA_{1c}.

2.7 | Statistical analysis

Paired-samples *t* tests were used for the analysis of biochemical and nutrient intake means. A one-way repeated-measures ANOVA was used to analyze the means for anthropometric, hemodynamic, and medication data. Significance was set at a P value of < 0.05. SPSS version 24 (IBM Corp., Armonk, NY) was used for data analysis.

3 | RESULTS

3.1 | Demographics

During screening, a total of 65 patients showed interest in participating in the study; however, 30 patients did not meet inclusion criteria or were excluded. Two individuals were unable to participate due to scheduling conflicts. Although 33 participants initially enrolled into the study, 2 participants were either lost to contact (n = 1) or no longer wished to follow the dietary protocol (n = 1). One participant refused to complete the final 24-hour dietary recall during week 4 due to time availability. Thus, a total of 31 participants provided clinical data and 30 participants provided nutrient intake data.

Based on clinical diagnoses and medical history, 33% of participants had coronary artery disease and 44% were either prediabetic (HbA_{1c} 5.7%–6.4%) or had diabetes mellitus ($HbA_{1c} \geq 6.5\%$; (Table 1). The average body mass index was 37.5 $kg/m^2 \pm 8.3$ kg/m^2, and approximately 81% of the participants were obese.

3.2 | Nutrient intake

Nutrient intake of participants on the defined, plant-based diet significantly changed after 4 weeks (Table 3). Significant reductions in energy intake, saturated fat as a percent of energy, dietary cholesterol, protein as a percent of energy, total fat, monounsaturated and polyunsaturated fat as a percent of energy, trans fat, vitamin D, vitamin B12, calcium, zinc, and sodium were observed after 4 weeks. Carbohydrate intake as a percent of energy, vitamin A, vitamin C, folate, dietary fiber, magnesium, and potassium intake increased significantly after 4 weeks. Patients anecdotally reported overall satisfaction with the food provided during the clinical follow-ups, and no significant symptoms of increased hunger were reported.

3.3 | Clinical variables

Anthropometric and hemodynamic characteristics, as well as medications, changed significantly ($P \leq 0.018$) from baseline to 4 weeks (Table 4). Adherence was well maintained over the 4-week period. Overall, participants were noncompliant for 3.6 out of 28 days. There were no significant differences between subjects with 100% adherence and lower-adherent subjects. Participants lost on average a total of 6.7 kg (14.7 lbs.) after 4 weeks on the defined plant-based diet (Table 4). SBP and DBP decreased by 16.6 mmHg and 9.1 mmHg, respectively. The reduction in blood pressure was accompanied with a decreased use of blood pressure medications (decreased 33% by week 4). Additionally, those taking hypoglycemic drugs, including insulin, reduced medication usage by 87%. Overall, total medication usage decreased 40% by week 4.

3.4 | Biomarkers

All biochemical changes were significant ($P \leq 0.037$) at 4 weeks compared with baseline, with the exception of the total cholesterol to high-density lipoprotein cholesterol ratio ($P = 0.068$) and glucose ($P = 0.25$; Table 5). Although fasting glucose was not significantly reduced, HbA_{1c} was significantly reduced ($P = 0.002$).

The distribution of high-interest clinical variable changes during the intervention are displayed in Supporting Information, Figure, in the online version of this article.

TABLE 3 Nutrient intake[b]

	Baseline	Final	Change, %[a]	*P* Value[c]
Energy, Kcal	2053 ± 873	1369 ± 488	−33 (−683 ± 808)	<0.0005
Fat, % of energy	36.4 ± 10.4	19.0 ± 8.9	−48 (−17.3 ± 12.8)	<0.0005
Saturated fat, % of energy	11.6 ± 4.5	3.8 ± 2.7	−67 (−7.7 ± 5.5)	<0.0005
Monounsaturated fat, % of energy	13.2 ± 4.8	7.0 ± 3.9	−47 (−6.2 ± 5.4)	<0.0005
Polyunsaturated fat, % of energy	8.4 ± 5.6	5.4 ± 2.7	−36 (−3.0 ± 3.5)	<0.0005
Omega-6, g	18.5 ± 11.1	6.0 ± 4.7	−67 (−12.4 ± 10.6)	<0.0005
Omega-3, g	2.11 ± 1.60	2.14 ± 1.95	1 (0.03 ± 2.16)	0.92
Omega-6/omega-3[d]	9.8 ± 3.7	4.3 ± 3.0	−56 (−5.5 ± 3.8)	<0.0005
Trans fat, g	2.25 ± 1.97	0.04 ± 0.09	−99 (−2.21 ± 2.00)	<0.0005
Cholesterol, mg	295.4 ± 211.7	12.2 ± 56.2	−96 (−283.2 ± 214.8)	<0.0005
Carbohydrate, % of energy	46.3 ± 14.0	72.6 ± 11.3	57 (26.3 ± 17.0)	<0.0005
Protein, % of energy	16.5 ± 6.4	7.5 ± 2.1	−54% (−9.0 ± 6.1)	<0.0005
Total fiber, g	20.4 ± 11.9	51.0 ± 17.7	150 (30.6 ± 17.8)	<0.0005
Total vitamin A activity, IU	8265 ± 9258	33387 ± 19052	303 (25 121 ± 21 876)	<0.0005
Vitamin D, IU	159.1 ± 154.3	12.3 ± 30.4	−92 (−146.8 ± 161.8)	<0.0005
Vitamin E, mg	9.9 ± 6.3	10.5 ± 5.6	6 (0.6 ± 6.4)	0.60
Vitamin C, mg	87.7 ± 108.8	412.7 ± 164.7	370 (325.0 ± 197.3)	<0.0005
Vitamin B12, μg	4.0 ± 1.9	0.3 ± 0.8	−92 (−3.6 ± 2.3)	<0.0005
Folate, μg	298 ± 229	741 ± 298	115 (343 ± 329)	<0.0005
Iron, mg	15.4 ± 7.2	15.3 ± 6.9	−1 (−0.1 ± 9.9)	0.97
Calcium, mg	796 ± 438	566 ± 279	−29 (−229 ± 527)	0.024
Sodium, mg	3730 ± 1783	839 ± 778	−76 (−2891 ± 1776)	<0.0005
Magnesium, mg	288.1 ± 119.9	488.1 ± 186.0	69 (200.0 ± 178.0)	<0.0005
Zinc, mg	12.2 ± 5.9	7.8 ± 3.4	−76 (−4.4 ± 7.0)	0.002
Potassium, mg	2668 ± 1190	5078 ± 1758	90 (2410 ± 1764)	<0.0005

Data are presented as mean ± standard deviation unless otherwise indicated.

[a] Data are presented as percent change (mean ± standard deviation).

[b] Data are for subjects who completed 24-hour recalls at both baseline and 4 weeks and do not include dietary supplements (n = 30).

[c] Paired samples *t* tests for within-group comparisons of changes from baseline to final values.

[d] Values indicate a ratio.

TABLE 4 Change of anthropometrics, hemodynamics, medications, and adherence over 4 weeks

	Baseline	Week 1	Week 2	Week 3	Week 4	*P* Value[a]
Weight, kg, mean ± SE	108.1 ± 5.1	105.4 ± 4.8[b]	103.9 ± 4.8[b]	102.6 ± 4.7[b]	101.4 ± 4.7[b]	<0.0005
BMI, kg/m^2	37.5 ± 1.4	36.5 ± 1.4[b]	36.0 ± 1.4[b]	35.6 ± 1.4[b]	35.2 ± 1.4[b]	<0.0005
WC, cm	111.9 ± 2.5	109.2 ± 2.5[b]	107.6 ± 2.5[b]	106.3 ± 2.5[c]	105.3 ± 2.5[b]	<0.0005
SBP, mm Hg	146.6 ± 2.8	131.9 ± 2.8[b]	127.0 ± 2.4	129.5 ± 1.9	130.0 ± 2.3	<0.0005
DBP, mm Hg	91.2 ± 1.3	81.5 ± 1.4[b]	79.0 ± 1.3	82.1 ± 1.2	82.1 ± 1.2	<0.0005
BP medications	1.6 ± 1.1	1.6 ± 1.0	1.4 ± 1.0[d]	1.1 ± 1.0[d]	1.0 ± 0.1	<0.0005
Heart rate, bpm	69.8 ± 1.8	71.8 ± 1.9	68.4 ± 1.7	68.1 ± 1.7	66.2 ± 1.2	0.018
Other prescription drugs	1.0 ± 1.4	1.0 ± 1.4	0.9 ± 1.5	0.6 ± 0.9	0.5 ± 0.9	0.008
Total medications	2.6 ± 2.0	2.7 ± 2.0	2.3 ± 2.0[d]	1.8 ± 1.6	1.6 ± 1.3	<0.0005
Adherence, d/wk[e]	—	6.32 ± 0.19	6.03 ± 0.25	6.06 ± 0.27	5.96 ± 0.27	0.531

Abbreviations: ANOVA, analysis of variance; BMI, body mass index; BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure; SE, standard error; WC, waist circumference.

[a] Repeated-measures 1-way ANOVA with a Greenhouse–Geisser correction due to violation of Mauchly's test of sphericity ($P > 0.05$).

[b] $P \leq 0.001$ compared with previous week.

[c] $P \leq 0.01$ compared with previous week.

[d] $P \leq 0.05$ compared with previous week (all pairwise comparisons were determined by post hoc analysis with a Bonferroni adjustment).

[e] Measured by weekly adherence-assessment tool. Values represent the number of days on average that adherence was 100% out of 1 week (7 days).

4 | DISCUSSION

Four weeks of a defined, plant-based dietary intervention resulted in clinically significant reductions in SBP, DBP, blood pressure medication usage, total medication usage, and serum lipids. Statistically significant reductions were also observed for other CVD risk factors, including body weight, heart rate, waist circumference, insulin, HbA_{1c}, and hs-CRP. This intervention demonstrated that a plant-based diet can be used effectively in the clinical setting with profound results. Additionally, subjects were able to transition from a standard American diet to the plant-based diet outlined in this intervention with good adherence. Physician advice can significantly impact the dietary choices of patients,[17] as demonstrated in this trial.

Although weight was reduced, this likely did not contribute fully to the reduction in blood pressure. A recent Cochrane review of randomized trials lasting ≥24 weeks examined the effects of weight loss on blood pressure and concluded that a 4-kg reduction in weight resulted in a 4.5-mmHg and 3-mmHg reduction in SBP and DBP, respectively.[18] Results from this review would underestimate expected outcomes of this trial. In comparison, participants in the present study lost 6.7 kg and reduced SBP and DBP by 16.6 mmHg and 9.1 mmHg, respectively. These findings are striking considering that blood pressure medications were reduced by 33% by week 4 and blood pressure nearly normalized. Participants' blood pressure was better even when discontinuing medications, which may indicate superiority of the dietary intervention over drug therapy. The reduction in blood pressure by this nutritional intervention was due to a variety of contributing factors, which may include a reduction in hs-CRP (−2.4 ± 3.7 mg/L)[19] and increased consumption of nitrates,[20] potassium,[21] and magnesium.[22] Increased dietary fiber,[23] phytosterols,[24] and polyphenols[25] also likely contributed to reduced serum lipids in addition to the exclusion of animal-based foods.[26]

It is interesting to note that fasting blood glucose was not significantly reduced ($P = 0.25$), yet HbA_{1c} was significantly reduced ($P = 0.002$). It is likely that reduced postprandial glucose fluctuations accounted for this decrease in HbA_{1c}, although this was not directly tested. It has been previously demonstrated that $HbA_{1c} < 7\%$ is mostly influenced by postprandial glucose.[27] The average HbA_{1c} of this sample was 5.9%; therefore, postprandial blood glucose would likely play a more significant role.

Other similar plant-based dietary trials have also demonstrated reduced CVD risk factors. In a 4-week randomized trial comparing a low-fat, plant-based diet to an American Heart Association diet, Macknin et al[28] reported significant reductions in weight (3.64 ± 3.41 kg), SBP (7.96 ± 12.28 mmHg), and LDL-C (27.00 ± 26.72 mg/dL) compared with baseline in adults on the plant-based diet. Bloomer et al[29] conducted a trial in which subjects consumed a plant-based diet for 3 weeks. Despite normal baseline clinical indicators, large reductions were observed in LDL-C (22.3 mg/dL), SBP (8.8 mmHg), and DBP (5.2 mmHg).

Jenkins et al[30] fed 3 weight-maintaining diets for 2 weeks that were low in saturated fat to participants with elevated LDL-C (~115 mg/dL at baseline). The dietary groups included a conventional low-fat diet, a vegetarian diet high in complex carbohydrates, and a raw vegan diet similar to that of the present study. Significant differences in changes of serum LDL-C were observed between these dietary groups. The conventional low-fat diet reduced LDL-C by 8 mg/dL, the starch-based vegetarian diet reduced LDL-C by 27 mg/dL, and the raw vegan diet reduced LDL-C by 38 mg/dL ($P < 0.001$). Thus, a raw plant-based diet may result in greater reductions in serum lipids than one that includes cooked complex carbohydrates.

TABLE 5 Change in biochemical variables after 4 weeks

	Baseline	Final	Change	*P* Value[a]
TC, mg/dL	216.6 ± 34.2	182.7 ± 29.9	−33.8 ± 25.9	<0.0005
LDL-C, mg/dL	143.0 ± 28.9	118.4 ± 26.4	−24.6 ± 21.3	<0.0005
HDL-C, mg/dL	54.8 ± 9.4	49.5 ± 10.6	−5.2 ± 6.2	<0.0005
TC/HDL[b]	4.04 ± 0.88	3.81 ± 0.88	−0.22 ± 0.64	0.068
TG, mg/dL	124.1 ± 58.1	104.5 ± 53.6	−19.6 ± 38.4	0.008
Insulin, uIU/mL	14.6 ± 7.6	10.3 ± 7.6	−4.2 ± 5.1	<0.0005
Glucose, mg/dL	90.1 ± 12.0	87.1 ± 4.7	−2.9 ± 14.0	0.25
HbA_{1c}, %	5.9 ± 0.5	5.7 ± 0.3	−0.2 ± 0.3	0.002
hs-CRP, mg/L	7.8 ± 6.4	5.3 ± 4.7	−2.4 ± 3.7	0.001

Abbreviations: HbA_{1c}, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; SD, standard deviation; TC, total cholesterol; TG, triglycerides. Data are presented as mean ± SD; n = 31.

[a] Paired-samples *t* tests for within-group comparisons of changes from baseline to final values.

[b] Values indicate a ratio.

4.1 | Study strengths and limitations

Several strengths of the present study should be noted. First, the utilization of the food classification system allows for reproducibility in other clinical practices and trials, as the food selection type, preparation, and degree of processing is detailed. Second, the utilization of a prescribed nutrition program in an outpatient cardiovascular clinic allows for the close assessment of the patient's clinical response to the diet. This was facilitated by weekly office visits that allowed for medication weaning as needed. In addition, the provision of food to participants helped facilitate adherence to the dietary protocol. Although there were no statistical differences between high- and low-adherent subjects, a lack of statistical power may be present due to a reduced sample size when groups were divided based on adherence. Additionally, strict adherence standards may also have required a larger sample size for statistical significance to be apparent between groups. A single bite or drink of any food outside of the prescribed diet counted against adherence for the day, even if the remainder of the day represented complete dietary compliance. Lastly, the range of reported dependent variables represents meaningful clinical indicators often evaluated in cardiology practices across the United States. These clinical indicators are most commonly used in the assessment of CVD risk. Thus, this study has real-world applicability in the clinical setting.

Limitations of the current study include the small sample size, lack of a control group, and short duration of follow-up. Although the sample size was small, the large effect sizes indicate that the sample size was more than sufficient for adequate power of the primary endpoints. Further research is needed to determine whether medications,

serum lipids, and blood pressure would continue to decrease if the diet were consumed for an extended period of time. In addition, extended trials are needed to assess long-term adherence to the diet. Lastly, inclusion of periodic postprandial glucose testing during the intervention may help establish a potential relationship between postprandial glucose fluctuations and reduced HbA_{1c}.

5 | CONCLUSION

A defined plant-based diet can be used as an effective therapeutic approach in the clinical setting in the treatment of HTN, hypercholesterolemia, and other cardiovascular risk factors while simultaneously reducing overall medication usage. Patients may find this therapeutic approach preferable to conventional and costly drug therapy. Further replication trials are needed with larger sample sizes, control groups, and other dietary comparison groups.

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Conflicts of interest

The authors declare no potential conflicts of interest.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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