

PAPER

Almonds vs complex carbohydrates in a weight reduction program

MA Wien¹, JM Sabaté², DN Iklé¹, SE Cole¹ and FR Kandeel¹

¹City of Hope National Medical Center, Duarte, CA, USA; and ²Loma Linda University, Loma Linda, CA, USA

OBJECTIVE: To evaluate the effect of an almond-enriched (high monounsaturated fat, MUFA) or complex carbohydrate-enriched (high carbohydrate) formula-based low-calorie diet (LCD) on anthropometric, body composition and metabolic parameters in a weight reduction program.

DESIGN: A randomized, prospective 24-week trial in a free-living population evaluating two distinct macronutrient interventions on obesity and metabolic syndrome-related parameters during weight reduction.

SUBJECTS: In total, 65 overweight and obese adults (age: 27–79 y, body mass index (BMI): 27–55 kg/m²).

INTERVENTION: A formula-based LCD enriched with 84 g/day of almonds (almond-LCD; 39% total fat, 25% MUFA and 32% carbohydrate as percent of dietary energy) or self-selected complex carbohydrates (CHO-LCD; 18% total fat, 5% MUFA and 53% carbohydrate as percent of dietary energy) featuring equivalent calories and protein.

MAIN OUTCOME MEASUREMENTS: Various anthropometric, body composition and metabolic parameters at baseline, during and after 24 weeks of dietary intervention.

RESULTS: LCD supplementation with almonds, in contrast to complex carbohydrates, was associated with greater reductions in weight/BMI (–18 vs –11%), waist circumference (WC) (–14 vs –9%), fat mass (FM) (–30 vs –20%), total body water (–8 vs –1%) and systolic blood pressure (–11 vs 0%), $P=0.0001$ –0.05. A 62% greater reduction in weight/BMI, 50% greater reduction in WC and 56% greater reduction in FM were observed in the almond-LCD as compared to the CHO-LCD intervention. Ketone levels increased only in the almond-LCD group (+260 vs 0%, $P<0.02$). High-density lipoprotein cholesterol (HDL-C) increased in the CHO-LCD group and decreased in the almond-LCD group (+15 vs –6%, $P=0.05$). Glucose, insulin, diastolic blood pressure, total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C) and LDL-C to HDL-C ratio decreased significantly to a similar extent in both dietary interventions. Homeostasis model analysis of insulin resistance (HOMA-IR) decreased in both study groups over time (almond-LCD: –66% and CHO-LCD: –35%, $P<0.0001$). Among subjects with type 1 diabetes, diabetes medication reductions were sustained or further reduced in a greater proportion of almond-LCD as compared to CHO-LCD subjects (96 vs 50%, respectively).

CONCLUSION: Our findings suggest that an almond-enriched LCD improves a preponderance of the abnormalities associated with the metabolic syndrome. Both dietary interventions were effective in decreasing body weight beyond the weight loss observed during long-term pharmacological interventions; however, the almond-LCD group experienced a sustained and greater weight reduction for the duration of the 24-week intervention. Almond supplementation of a formula-based LCD is a novel alternative to self-selected complex carbohydrates and has a potential role in reducing the public health implications of obesity.

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Keywords: nuts; almonds; obesity; metabolic syndrome; insulin resistance; type 2 diabetes; weight loss

*Correspondence: Dr MA Wien, Department of Diabetes, Endocrinology and Metabolism, City of Hope National Medical Center, 1500 East Duarte Road, Duarte, CA 91010, USA.

E-mail: mwien@coh.org

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Introduction

The epidemic of overweight and obesity among affluent nations is fueling the increasing prevalence of the metabolic syndrome and type II diabetes, which has serious implications for healthcare systems and the economy. Metabolic syndrome encompasses a cluster of abnormalities including insulin resistance, central obesity, hypertension and dyslipidemia.¹ Both type 2 diabetes and the insulin resistance syndrome are associated with a marked increased risk for

cardiovascular disease (CVD)² and have become a significant clinical challenge for practitioners. Contributors to these conditions are improper nutrition and inadequate physical activity; thus weight management is a cornerstone of treatment and prevention.

The effects of dietary fat on adiposity have been intensively debated in recent years. Obesity experts have argued that habitual consumption of fatty diets contributes to the development and maintenance of excess body weight.^{3–8} Others have noted that diets high in fat do not appear to be the primary cause of the high prevalence of excess body fat within the United States (US).⁹ Emphasis on dietary fat reduction within the US public health dietary guidelines has yielded an increased consumption of processed grains, reduced-fat and fat-free products.¹⁰ Failure to consider portion sizes and total energy intake during the past two decades has contributed towards an increased risk for obesity, type 2 diabetes and CVD.^{11,12}

According to a recent meta-analysis from the Cochrane Collaboration, low-fat diets (20% of energy or less) have poor clinical effectiveness in the outpatient treatment of obesity.¹³ Obese individuals enrolled in long-term weight reduction programs frequently maintain a steady state after 12 weeks of dietary intervention,¹⁴ possibly due to waning compliance and diminished energy requirements.^{15,16} An ideal weight reduction dietary regimen would create an optimal hormonal milieu to improve the obese individual's metabolic abnormalities,¹⁷ mobilize abdominal adipose tissue and promote compliance. Thus, studies examining the effects of other dietary macronutrient compositions and modifications to the traditional formula-based LCD are of considerable scientific and public health interest.

Dietary fatty acids (saturated, mono- and poly-unsaturated) are unequal in their ability to improve metabolic parameters associated with the metabolic syndrome and coronary heart disease (CHD).¹⁸ Previous studies featuring isocaloric diets have shown that plasma concentrations of total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) typically improve when monounsaturated fat (MUFA) replaces saturated fat in dietary patterns.^{19,20} Incorporating a preponderance of MUFA under hypocaloric conditions may further improve the metabolic syndrome through multiple mechanisms, for example, decreased triacylglycerol concentrations,²¹ decreased LDL-C to HDL-C ratio¹⁴ and attenuated day-long hyperinsulinemia.^{22,23} In an effort to reduce the incidence of CHD, the current National Cholesterol Education Program guidelines²⁴ emphasize a more liberal approach in total and MUFA consumption, similar to Mediterranean food patterns (total fat = 40–45% of energy, rich in MUFA (specifically oleic acid)). In addition to their high levels of MUFA, and to a lesser degree polyunsaturated fatty acids (PUFA), nuts have been shown through epidemiological^{25,26} and interventional studies^{27–33} to confer beneficial effects on reducing cardio-

vascular risk. The possible association between high PUFA diets and carcinogenesis,^{34,35} in addition to potential palatability and compliance issues, pre-empted consideration of enriching a formula-based low-calorie diet (LCD) with large amounts of a high PUFA oil. In light of their high levels of oleic acid, as well as textural characteristics, whole unblanched unsalted almonds were chosen to evaluate their influence on anthropometric, body composition and metabolic parameters in one of two different enriched formula-based LCDs (complex carbohydrate or almond) during a 24-week weight reduction intervention.

Methods

Study design

Subjects were recruited from the pool of outpatients entering into the 24-week Diabetes and Cardiovascular Risk Reduction Program (D & CVRRP) for medically supervised weight reduction at City of Hope (COH) National Medical Center in Duarte, California. Acceptance into the D & CVRRP requires a medical diagnosis that can be ameliorated or improved by weight reduction, age ≥ 18 y, and body mass index (BMI) ≥ 25 kg/m². Patients on lipid-lowering medications and women receiving hormone replacement therapy were excluded from study participation. The study was conducted from February 2000 to May 2002. The study protocol was approved by the Institutional Review Boards of COH and Loma Linda University and all participants gave written informed consent.

Subjects were randomized to consume almonds (almond-LCD) or self-selected complex carbohydrates (CHO-LCD) using computer generated Random Number Generation software (RNDGEN, Stanford, USA) with stratification according to gender and physician documented presence or absence of type 2 diabetes. Study recruitment led to a population of male and female subjects with BMI ranging from 27 to 55 kg/m² and a median age of 55 y (range 27–79 y). In total, 65 subjects were randomized into the two intervention groups (Figure 1) and 52 patients completed the 24-week study. The number of withdrawals from the two groups was similar, eight from the almond-LCD group and five from the CHO-LCD group. Primary reasons for withdrawal included work and time conflicts. No significant difference in baseline demographic, anthropometric or metabolic characteristics were found in the two intervention groups after randomization (Table 1).

The total dietary intervention period for each subject was 24 weeks, preceded by a 2-week run-in with no intervention other than a multivitamin/mineral supplement. Subjects consumed a formula-based LCD supplemented with 84 g/day almonds or self-selected complex carbohydrates and safflower oil (see below). The two study groups had distinctly different levels of total and MUFA; however, both groups were equally balanced on total calories, protein, cholesterol and saturated fat (Table 2). Health Management Resources

Initial Run-In Period on Multivitamin/mineral Supplement (2 weeks)

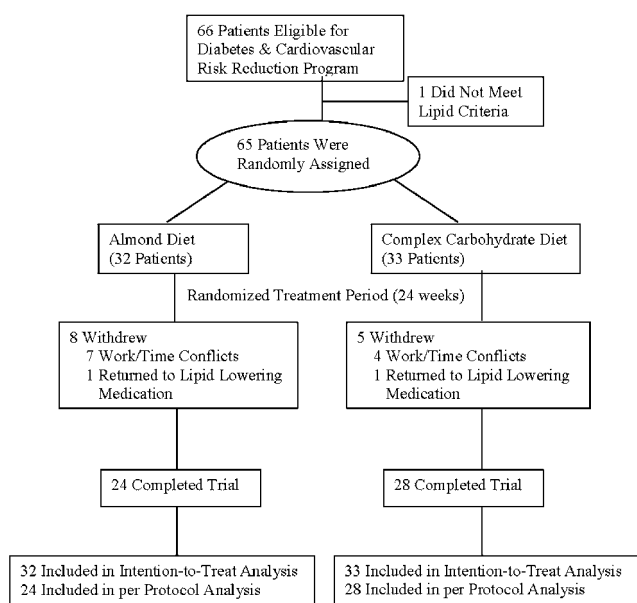


Figure 1 Flow of patients throughout the trial.

(HMR) 70 Plus, a protein-sparing formulation prescribed during LCDs to ameliorate the loss of lean body mass, was prescribed according to D&CVRRP guidelines. Subjects were instructed to mix the HMR powder according to package instructions and to consume two HMR vitamin/mineral supplements and D&CVRRP ‘protocol’ salad daily. Almond-LCD subjects were given weekly allotments of prepackaged whole unblanched unsalted almonds. The amount of almonds was selected based on published data reporting favorable changes in blood lipids incorporating this amount of almonds under isocaloric conditions. Almond-LCD subjects were advised to consume the almonds at the time of day most convenient to their lifestyle. CHO-LCD subjects were given explicit instructions on how to self-select a combination of complex carbohydrates daily from a food list that were equivalent in calories to 84g almonds. The food list featured a wide range of glycemic index complex carbohydrate-containing foods (peas, corn, potato, pasta, rice, etc). Additionally, CHO-LCD subjects were instructed to consume two teaspoons of safflower oil daily to meet essential fatty acid requirements. Energy and nutrient composition of the diets were computed using Food Processor (Version 7.11, ESHA Research, Salem, OR, USA).

Subjects completed detailed daily food and exercise records in their weekly D & CVRRP logbooks. The Program Dietitian performed weekly face-to-face reviews of the records and suggestions to enhance compliance were provided. Subjects were advised to refrain from exercise during the first 4 weeks of the D & CVRRP to allow time for

Table 1 Characteristics at baseline for all randomized subjects

	Almond-LCD ^a (n = 32)	Carbohydrate-LCD (n = 33)
Age (y)	53 ± 2	57 ± 2
Sex, n (%)		
Female	19 (59%)	18 (55%)
Male	13 (41%)	15 (45%)
Ethnicity, n (%)		
Caucasian	20 (63%)	22 (67%)
Hispanic	4 (13%)	6 (18%)
African American	7 (21%)	1 (3%)
Asian	1 (3%)	4 (12%)
Weight (kg)	113 ± 5	114 ± 5
BMI (kg/m ²)	39 ± 1	37 ± 1
FM (%)	42 ± 2	43 ± 2
WC (cm)	122 ± 5	117 ± 5
Blood pressure (mmHg)		
Systolic	145 ± 4	138 ± 3
Diastolic	77 ± 2	78 ± 2
Plasma lipids (mg/dl) ^b		
Total cholesterol	198 ± 8	216 ± 7
LDL cholesterol	99 ± 5	108 ± 5
HDL cholesterol	33 ± 2	33 ± 2
Triglycerides	180 ± 19	193 ± 16
Glucose (mg/dl) ^b	152 ± 12	152 ± 12
Insulin (μU/ml)	46 ± 8	47 ± 6

^aValues are means ± s.d.

^bTo obtain mmol/l values for LDL and HDL cholesterol, multiply values by 0.0259; for triglycerides, multiply values by 0.0113; and for glucose multiply values by 0.0555.

Table 2 Energy and nutrient composition of the intervention diets^a

	Almond-LCD	Carbohydrate-LCD
Energy (kcal) ^b	1012	1015
Protein (% of energy)	29	29
Carbohydrates (% of energy)	32	53
Fat (% of energy)	39	18
Saturated fatty acids	3	3
Monounsaturated fatty acids	25	5
Polyunsaturated fatty acids	11	10
Cholesterol (mg)	4	4
Dietary fiber (g)	20	32

^aBased on calculated nutrient composition of the prescribed diet protocols using Food Processor (Version 7.11, ESHA Research, Salem, OR, USA).

^bTo convert values for total energy from kilocalories (kcal) to kilojoules (kJ), multiply by 4.184.

LCD = low-calorie diet.

adaptation to the LCD, and then subsequently were encouraged to walk for 20–30 min three to five times per week. Excessive deviations were operationally defined as failure to stay within 25% of the weekly prescribed calories

and minutes of activity, which prompted additional individualized sessions with the Program Psychologist and/or Program Dietitian. Both groups had equivalent levels of noncompliance necessitating the aforementioned sessions during the 24-week intervention.

Clinical assessments were made at the 24 consecutive weekly visits during normal D & CVRRP outpatient clinic operations. All subjects attended weekly clinic visits with an endocrinologist, followed by nutrition and behavior modification classes. Weight, blood pressure (BP) and heart rate were measured weekly using calibrated office instruments, and ketone levels were taken using a Hemocue™ monitor. Body weight was determined to the nearest 0.1 kg. Plasma lipids, insulin and glucose were measured at baseline (week 0) and at weeks 8, 16 and 24. Additionally, subjects were asked to subjectively evaluate and record the acceptability of their prestudy diet and their assigned study intervention at weeks 8, 16 and 24, in terms of satiety, palatability and texture using a 0–10-point semantic scale (0, not satisfied at all; 5, neutral; and 10, very satisfied).

Venous blood was collected after an overnight fast at the General Clinical Research Center (GCRC) unit at COH. The University of Southern California Core Lipid Laboratory performed the lipid panel and Lipoprotein Quantification (LPQ) analysis. Plasma was analyzed using the Centers for Disease Control certified Lipid Research Clinics Protocol³⁶ for TC, TG and HDL-C after dextran sulfate–magnesium chloride preparation. LPQ was performed for direct evaluation of HDL-C and LDL-C using a COBAS MIRAS analyzer (Roche). Insulin concentrations were determined by human specific radioimmunoassay (Linco St. Charles, Missouri) methodology and glucose concentrations were measured by a Stat Glucose/Lactate Analyzer Model 2000 (YSI, Yellow Springs, OH, USA).

Additional anthropometric assessments were performed at baseline and at week 24, including bioelectrical impedance analysis using the Tanita® TBF-300 body composition analyzer/scale and waist measurements. The Tanita® analyzer/scale utilizes ‘foot-to-foot’ pressure contact electrode technology to determine internal body composition,³⁷ which others have validated in the obese population.³⁸ A proprietary algorithm derives the percent body fat by combining impedance and weight measurements with height, gender, age and physical activity level. BMI was calculated as weight(kg)/height(m²). WC positively correlates with metabolic syndrome-related atherogenic lipid abnormalities among obese individuals.³⁹ WC measurements were made to the nearest 0.1 cm, midway between the last rib and the ileac crest, to estimate the change in visceral fat in the abdominal region.

Homeostasis model analysis⁴⁰ (HOMA) was utilized to estimate the change in insulin resistance (HOMA-IR) from fasting glucose and insulin concentrations. HOMA-IR was calculated using the formula $[\text{insulin}(\text{pM}) \cdot \text{glucose}(\text{mM})] / 22.5$.⁴⁰

Statistical analysis

Sample size and power calculations were performed utilizing UnifyPower Macro for SAS. Data were entered into a JMP database and statistical analysis was performed using SAS software (JMP Version 4.0.5, and, SAS Version 8.2; SAS Institute, Cary, NC, USA). Two-sided unpaired *t*-tests were performed on all subject baseline characteristics using a probability value of 0.05. In light of the longitudinal structure of the data, a mixed model with an autoregressive covariance structure of lag 1 was used to test all hypotheses, including those involving multiple covariates. All percent change values presented are least-squares means estimated from mixed models. The effect of each treatment on each end point over time was plotted as the least-squares mean and 95% CI by treatment group over time for each end point. Models were adjusted for baseline measurements, and all time points (0, 8, 16, and 24 weeks) were included in the analysis, with the exception of weight and BMI which included data from all 24 weeks. Both an intent-to-treat and as-treated analysis were performed and produced similar findings. Thus, the intent-to-treat data, which is the least biased analysis, are presented within this paper. The assumption used in the intent-to-treat model with regard to unmeasured end points for the dropouts was that they were missing at random.

Results

Results are presented based on percent change in least-squares means (Table 3). The study sample size did not allow for evaluation of the ethnic diversity of this cohort.

Anthropometrics and body composition

Figure 2 shows the weekly change in body weight during the 24-week intervention. Almond consumption was associated with greater reduction in weight/BMI (–18 vs –11%, $P < 0.0001$), WC (–14 vs –9%, $P < 0.05$), fat mass (FM) (–30 vs –20%, $P < 0.05$) and total body water (TBW) (–8 vs 1%, $P < 0.05$). Neither gender nor chronic disease (type 2 diabetes mellitus, hypertension) were independently responsible for the weight difference found between the two groups. A divergence in weight loss between groups occurred at week 16 of the intervention, at which time the CHO-LCD group experienced a ‘plateau’. In the CHO-LCD group, 92% of the total weight loss was seen in the first 16 weeks of the intervention in contrast to the almond-LCD group which experienced 77% of the total weight loss by week 16. Both interventions were associated with a decline in fat-free mass (FFM) over the study period ($P < 0.0001$); however, no difference was found between the study groups.

Metabolic factors

Both study interventions were associated with similar declines in mean fasting insulin and glucose concentrations

Table 3 Summary statistics^a for anthropometric and metabolic parameters

Parameter	Week	Almond-LCD LSM (s.e.) (n = 32)	Carbohydrate-LCD LSM (s.e.) (n = 33)	% Change = week 24–week 0	
				Week 0	
				Almond-LCD	Carbohydrate-LCD
Weight (lbs)	0	244.7 (1.8)	244.7 (1.8)	–18***	–11
	24	201.7 (2.3)	218.1 (2.2)		
BMI (kg/m ²)	0	38.3 (0.3)	38.4 (0.3)	–18***	–11
	24	31.6 (0.3)	34.2 (0.3)		
WC (cm)	0	120 (1.0)	120 (1.0)	–14*	–9
	24	103 (1.3)	108 (1.3)		
FM (lbs)	0	102.6 (2.2)	102.1 (2.2)	–30*	–20
	24	71.5 (2.5)	82.1 (2.4)		
FFM (lbs)	0	138.0 (1.4)	137.4 (1.4)	–8	–4
	24	126.8 (1.6)	132.0 (1.5)		
TBW (lbs)	0	100.1 (1.4)	99.0 (1.4)	–8*	–1
	24	92.2 (1.6)	97.6 (1.6)		
Insulin (μU/ml)	0	46 (5)	47 (5)	–54	–32
	24	21 (5)	32 (5)		
Glucose (mg/dl)	0	152 (11)	152 (11)	–16	–16
	24	128 (11)	127 (11)		
HOMA-IR	0	20 (4)	17 (4)	–66	–35
	24	7 (2)	11 (2)		
Systolic BP (mmHg)	0	143 (3)	140 (3)	–11**	0
	24	127 (3)	138 (3)		
Diastolic BP (mmHg)	0	77 (2)	78 (2)	–8	–8
	24	71 (1)	72 (1)		
Ketone (mmol/l)	0	0.10 (.04)	0.11 (.03)	+260**	0
	24	0.36 (.05)	0.11 (.05)		
TC	0	198 (7)	216 (8)	–13	–9
	24	173 (8)	197 (8)		
TG	0	180 (17)	193 (17)	–29	–27
	24	128 (18)	141 (17)		
LDL-C	0	99 (5)	108 (5)	–15	–10
	24	84 (5)	97 (5)		
HDL-C	0	33 (2)	33 (2)	–6*	+15
	24	31 (2)	38 (2)		
LDL-C: HDL-C	0	3.1 (0.2)	3.5 (0.2)	–10	–23
	24	2.8 (0.2)	2.7 (0.2)		

^aAll outcome variables were adjusted for their baseline values in the models. *P*-values are based on mixed models with an autoregressive covariance structure of order one, with all time points (weeks 0, 8, 16 and 24) included in the model.

Indicates statistically significant difference between groups: ***(*P*<0.0001), **(*P*<0.02), and *(*P*<0.05).

LCD = low-calorie diet; LSM = least-squares means; and, s.e. = standard error.

(insulin: *P*<0.0001; and, glucose *P*<0.001) and were associated with decreases in HOMA-IR (*P*<0.0001). Diastolic BP decreased similarly by 8% in both interventions. Almond consumption was associated with a decrease in systolic BP as compared to no observed change within the CHO-LCD group (–11 vs 0%, *P*<0.01). Ketone levels increased significantly in the almond-LCD intervention compared to the CHO-LCD intervention (+260 vs 0%, *P*<0.02). TC and TG levels decreased over time in both groups (*P*<0.001 and 0.0001, respectively), but did not show significant variations between the two interventions. LDL-C decreased significantly in the almond-LCD and CHO-LCD interventions over time (–15 vs –10%, *P*<0.0001, respectively). Although HDL-C increased only in the CHO-LCD group compared to the

almond-LCD group (+15 vs –6%, *P*<0.05), the LDL-C to HDL-C ratio decreased (*P*<0.01) equivalently in both groups (*P*=NS).

Additional testing on hematological and biochemical laboratory parameters was performed at weeks 0, 12 and 24 according to D & CVRRP guidelines. No clinically significant changes in electrocardiogram, complete blood count, basic metabolic panel, uric acid, liver enzymes, total protein, albumin, calcium or total bilirubin occurred during the study.

Self-reported satiety and acceptability

Subjects did not differ in their self-reported evaluation of the acceptability of their assigned dietary intervention in terms

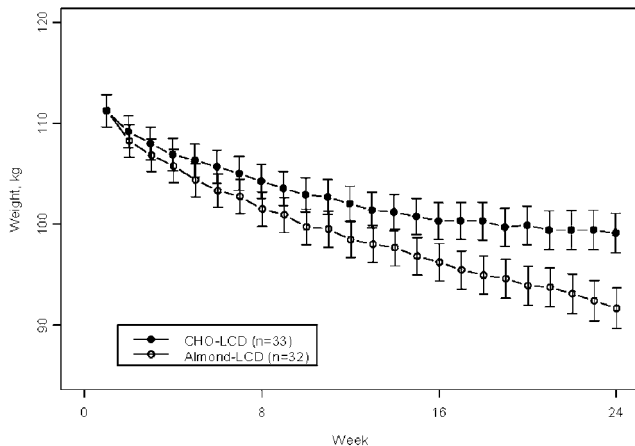


Figure 2 Weekly change in weight in the two study groups^a. ^aData are least-squares means and 95% CI; CHO = carbohydrate; LCD = low-calorie diet.

of satiety, palatability and texture at weeks 0, 8, 16 and 24. There were no significant differences between or within the groups over time. Hence, both almonds and complex carbohydrates were reported to be as satiating and satisfying as the subject's respective baseline diets.

Discussion

The present study was designed to evaluate two distinct macronutrient approaches in the context of a formula-based LCD and their subsequent impact on anthropometric, body composition and metabolic parameters during a 24-week weight reduction program in overweight and obese adults. Both nutritional interventions were effective in decreasing body weight beyond the weight loss observed during long-term interventions with sibutramine hydrochloride.⁴¹ The CHO-LCD group reached a plateau at week 16, similar to the onset of plateaus shown while using intermittent and continuous sibutramine therapy.⁴¹ However, the almond-LCD group experienced a sustained and greater weight reduction for the duration of the 24-week intervention. A 62% greater reduction in weight/BMI, 50% greater reduction in WC, and 56% greater reduction in FM were observed in the almond-LCD as compared to the CHO-LCD intervention. The decreases in FFM between the two interventions were similar, whereas TBW decreased significantly more in the almond-LCD group.

The difference in weight loss was unexpected, given the study design featuring a matched prescribed total calorie intake and equivalent levels of self-reported physical activity between the groups. Neither gender, presence of type 2 diabetes mellitus nor hypertension influenced the magnitude of the difference in weight change. McManus *et al*⁴² have shown that higher fat diets may be more satiating than lower fat diets containing high glycemic index foods. Others

have noted that unanticipated weight loss occurs in controlled feeding trials featuring the inclusion of nuts under isocaloric conditions.^{43,44} The fiber matrix of the nut may have compromised the absorption of the fat from the almonds yielding an imbalance of energy sources between the groups. These data suggest that the greater weight loss observed in almond consumers may have been secondary to greater satiety and the lower bioavailability of calories from nuts.

A greater improvement of fasting glucose and insulin using a hypocaloric low carbohydrate diet enhanced with MUFA has been reported.⁴⁵ Our MUFA-enriched almond intervention showed an overall 54% reduction in fasting insulin, as compared to a 32% reduction in the carbohydrate intervention, in the context of an unequal magnitude of weight loss. Comparison of a subject's fasting glucose and insulin concentrations within the HOMA-IR prediction model provides a quantitative assessment of the contribution of insulin resistance to the fasting metabolic state.⁴⁰ A 31% difference in the magnitude of HOMA-IR reduction occurred between the two study groups (almond-LCD: -66% and CHO-LCD: -35%). Almond consumption was associated with improved insulin sensitivity, which might have produced a compensatory reduced load on the pancreas. Also, the high oleic acid content in the almonds may have contributed to improved β -cell efficiency through enhanced intestinal secretion of glucagon-like-peptide-1 (GLP-1).⁴⁶ Enhancing the β -cell secretory response by dietary measures will improve the regulation of postprandial glucose disposal and insulin sensitivity,⁴⁷ which has the potential for improving the cluster of abnormalities linked to the metabolic syndrome.⁴⁸ Further, among subjects with type 2 diabetes, diabetes medication reductions were sustained or further reduced in a greater proportion of almond-LCD as compared to CHO-LCD subjects (96 vs 50%, respectively).

Hypertensive patients in both groups experienced reductions in their antihypertensive medications during the 24-week study. However, there were more patients in the CHO-LCD group (62%) than in the almond-LCD group (50%) with documented hypertension at baseline. Thus, it is possible that the absence of a reduction in systolic BP within the CHO-LCD group may have been due to better BP control at baseline secondary to antihypertensive therapy.

The change in the hormonal milieu that occurs in the presence of high-fat diets may have favorably improved the utilization of adipose fat stores as an energy source in the almond intervention. The higher ketone levels in the almond-LCD group were anticipated due to the higher proportion of energy from total fat (almond-LCD: total fat = 39% of energy, CHO-LCD: total fat = 18% of energy). The increased production of ketones within the almond-LCD group may reflect a higher rate of fat breakdown that exceeded the level at which the tissues could oxidize the fat intermediates for energy production and some calories may have been lost through ketonuria. Also, a small proportion of the difference in the magnitude of weight loss in the

almond-LCD group may have been due to ketosis-induced diuresis in the context of the significantly greater loss of FM.

Similar decreases in TC levels were observed in the context of an unequal magnitude of weight loss between the two interventions. TG levels decreased in a sustainable manner in both groups over the 24-week intervention in contrast to others who have noted a transient increase in TG levels in subjects treated with hypocaloric diets.⁴⁹ The almond-LCD group experienced a reduction in LDL-C from baseline by 15% as compared to a 10% reduction in the CHO-LCD group. Under isocaloric conditions, other investigators have found similar dose responses using almonds to reduce LDL-C, for example, 1% for every 7,^{27,30} 8^{31,50} and 10 g/day.⁵¹

HDL-C concentrations have been shown to vary dependent on whether subjects are studied during an acute weight-loss phase as compared to a reduced and stable weight.⁵² During acute weight reduction tissue concentrations of lipoprotein lipase decrease by 50–80%⁴⁹ resulting in reduced TG-rich lipoprotein synthesis, impaired very-LDL-C catabolism, and diminished transfer of lipids to HDL-C, and, therefore reduced HDL-C concentrations. Although HDL-C did not increase in the almond-LCD group, the LDL-C to HDL-C ratio, an important predictor of cardiovascular risk,⁵³ decreased equivalently in both groups. Jenkins *et al*²⁷ found a 12% reduction in the LDL-C to HDL-C ratio using 73 g/day almonds under isocaloric conditions in hypercholesterolemic subjects (BMI: 20–32 kg/m²), whereas our study found a 10% reduction using 84 g/day under hypocaloric conditions in overweight and obese subjects (BMI: 27–55 kg/m²). These studies complement each other as they have produced diminished cardiovascular risk using liberal amounts of total fat (specifically MUFA) among different high-risk patient populations, and have produced findings that are consistent with epidemiologic data that has found nut consumption to be associated with reduced CHD risk.^{54,55}

Zambon *et al*¹⁴ found that LDL-C decreased significantly in a group of obese normolipemic premenopausal women consuming hypocaloric diets enriched in olive oil (MUFA) and complex carbohydrates. However, with an equal magnitude of weight loss (–11% in both groups), HDL-C increased significantly in the high MUFA group and decreased in the complex carbohydrate group.¹⁴ Our study is unique from others in that it addressed the effect of almonds as a source of MUFA (specifically oleic acid) compared to complex carbohydrate in the context of a formula-based LCD, and featured equivalent levels of calories, protein, saturated fat and PUFA in the two interventions. In light of the wide range of self-selected glycemic index foods, we are unable to explain the rise in HDL-C in the CHO-LCD group. The difference in HDL-C between groups may be partially attributed to the difference in daily fiber intake (almond-LCD = 20 g, CHO-LCD = 32 g).

The present study demonstrates that the use of almonds in the context of a formula-based LCD is a feasible option for consideration and has a potential role in the public health implications of obesity. A primary complaint among over-

weight and obese subjects participating in formula-based medically supervised weight reduction programs is the lack of texture variability and satiety. If clinicians are capable of sustaining motivation and compliance using nuts, a successful formula-based LCD could contain larger proportions of MUFA. However, careful patient monitoring is required to ensure that there is improvement in metabolic parameters in parallel to weight reduction. Our findings call for additional studies in larger numbers of subjects to allow evaluation of different fat to CHO ratios and whether consumption of almonds (or other nuts) as the delivery vehicle were responsible for the disparity in weight loss. The use of almonds to ameliorate the recidivism commonly observed after active weight reduction is also worthy of exploration.

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References

- 1 Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA* 2002; **287**: 356–359.
- 2 Kendall DM, Harmel AP. The metabolic syndrome, type 2 diabetes, and cardiovascular disease: understanding the role of insulin resistance. *Am J Manage Care* 2002; **8**(20 Suppl): S635–S653; quiz S654–S637.
- 3 Pi-Sunyer FX. Effect of the composition of the diet on energy intake. *Nutr Rev* 1990; **48**: 94–105.
- 4 Lissner L, Heitmann BL. Dietary fat and obesity: evidence from epidemiology. *Eur J Clin Nutr* 1995; **49**: 79–90.
- 5 Grundy SM. Multifactorial causation of obesity: implications for prevention. *Am J Clin Nutr* 1998; **67**(3 Suppl): S635–S72S.
- 6 Shah M, Garg A. High-fat and high-carbohydrate diets and energy balance. *Diabetes Care* 1996; **19**: 1142–1152.
- 7 Sclafani A. Obesity. In: Brodoff B (ed.) *Dietary obesity models*. JB Lippincott: Philadelphia; 1992, pp 241–248.
- 8 Popkin BM, Paeratakul S, Zhai F, Ge K. A review of dietary and environmental correlates of obesity with emphasis on developing countries. *Obes Res* 1995; **3** (Suppl 2): 145s–153s.
- 9 Willett WC, Leibel RL. Dietary fat is not a major determinant of body fat. *Am J Med* 2002; **113** (Suppl 9B): 47S–59S.
- 10 Yang EJ, Chung HK, Kim WY, Kerver JM, Song WO. Carbohydrate intake is associated with diet quality and risk factors for cardiovascular disease in US adults: NHANES III. *J Am Coll Nutr* 2003; **22**: 71–79.
- 11 Ludwig DS. The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. *JAMA* 2002; **287**: 2414–2423.
- 12 Willett WC. Dietary fat plays a major role in obesity: no. *Obes Rev* 2002; **3**: 59–68.
- 13 Pirozzo S, Summerbell C, Cameron C, Glasziou P. Advice on low-fat diets for obesity. *Cochrane Database Syst Rev* 2002; CD003640, 1–26.

- 14 Zambon A, Sartore G, Passera D, Francini-Pesenti F, Bassi A, Basso C, Cambon S, Nanzato E, Grepeldi G. Effects of hypocaloric dietary treatment enriched in oleic acid on LDL and HDL subclass distribution in mildly obese women. *J Intern Med* 1999; **246**: 191–201.
- 15 Leibel RL, Hirsch J. Diminished energy requirements in reduced-obese patients. *Metabolism* 1984; **33**: 164–170.
- 16 Weigle DS, Sande KJ, Iverius PH, Monsen ER, Brunzell JD. Weight loss leads to a marked decrease in nonresting energy expenditure in ambulatory human subjects. *Metabolism* 1988; **37**: 930–936.
- 17 Riccardi G, Rivellese AA. Dietary treatment of the metabolic syndrome—the optimal diet. *Br J Nutr* 2000; **83** (Suppl 1): S143–S148.
- 18 Keys A, Anderson JT, Grande F. Prediction of serum-cholesterol responses of man to changes in fats in the diet. *Lancet* 1957; **2**: 959–966.
- 19 Mensink RP, Katan MB. Effect of a diet enriched with mono-unsaturated or polyunsaturated fatty acids on levels of low-density and high-density lipoprotein cholesterol in healthy women and men. *N Engl J Med* 1989; **321**: 436–441.
- 20 Mattson FH, Grundy SM. Comparison of effects of dietary saturated, monounsaturated, and polyunsaturated fatty acids on plasma lipids and lipoproteins in man. *J Lipid Res* 1985; **26**: 194–202.
- 21 Grundy SM. Comparison of monounsaturated fatty acids and carbohydrates for lowering plasma cholesterol. *N Engl J Med* 1986; **314**: 745–748.
- 22 Reaven G. Metabolic syndrome: pathophysiology and implications for management of cardiovascular disease. *Circulation* 2002; **106**: 286–288.
- 23 Garg A. High-monounsaturated fat diet for diabetic patients. Is it time to change the current dietary recommendations? *Diabetes Care* 1994; **17**: 242–246.
- 24 Expert Panel in Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) (Adult Treatment Panel III). *JAMA* 2001; **285**: 2486–2497.
- 25 Sabate J. Nut consumption, vegetarian diets, ischemic heart disease risk, and all-cause mortality: evidence from epidemiologic studies. *Am J Clin Nutr* 1999; **70**: 500S–503S.
- 26 Lavedrine F, Zmirou D, Ravel A, Balducci F, Alary J. Blood cholesterol and walnut consumption: a cross-sectional survey in France. *Prev Med* 1999; **28**: 333–339.
- 27 Jenkins DJA, Kendall CWC, Marchie A, Parker TL, Connelly PW, Qian W, Haight JS, Faulkner D, Vidgen E, Lapsley KG, Spiller GA. Dose response of almonds on coronary heart disease risk factors: blood lipids, oxidized low-density lipoproteins, lipoprotein(a), homocysteine, and pulmonary nitric oxide. *Circulation* 2002; **106**: 1327–1332.
- 28 Sabate J, Fraser GE, Burke K, Knutsen SF, Bennett H, Lindstedt KD. Effects of walnuts on serum lipid levels and blood pressure in normal men. *N Engl J Med* 1993; **328**: 603–607.
- 29 Chisholm A, Mann J, Skeaff M. A diet rich in walnuts favourably influences plasma fatty acid profile in moderately hyperlipidaemic subjects. *Eur J Clin Nutr* 1998; **52**: 12–16.
- 30 Spiller GA, Jenkins DA, Bosello O, Gates JE, Cragen LN, Bruce B. Nuts and plasma lipids: an almond-based diet lowers LDL-C while preserving HDL-C. *J Am Coll Nutr* 1998; **17**: 285–290.
- 31 Spiller GA, Jenkins DJ, Cragen LN, Gates JE, Bosello O, Berra K, Radd C, Stevenson M, Superko R. Effect of a diet high in monounsaturated fat from almonds on plasma cholesterol and lipoproteins. *J Am Coll Nutr* 1992; **11**: 126–130.
- 32 Morgan WA, Clayshulte BJ. Pecans lower low-density lipoprotein cholesterol in people with normal lipid levels. *J Am Diet Assoc* 2000; **100**: 312–318.
- 33 O'Byrne DJ, Knauft DA, Shireman RB. Low fat-monounsaturated rich diets containing high-oleic peanuts improve serum lipoprotein profiles. *Lipids* 1997; **32**: 687–695.
- 34 Bagga D, Anders KH, Wang HJ, Glaspy JA. Long-chain n-3-to-n-6 polyunsaturated fatty acid ratios in breast adipose tissue from women with and without breast cancer. *Nutr Cancer* 2002; **42**: 180–185.
- 35 Kromhout D. The importance of N-6 and N-3 fatty acids in carcinogenesis. *Med Oncol Tumor Pharmacother* 1990; **7**: 173–176.
- 36 Lipid Research Clinics. *Manual of laboratory operations. Lipid and lipoprotein analysis (revised)*. US Government Printing Office, US Department of Health and Human Services: Washington, DC; 1982.
- 37 Nunez C, Gallagher D, Visser M, Pi-Sunyer FX, Wang Z, Heymsfield SB. Bioimpedance analysis: evaluation of leg-to-leg system based on pressure contact footpad electrodes. *Med Sci Sports Exerc* 1997; **29**: 524–531.
- 38 Hainer V, Kunesova M, Parizkova J, Stich V, Horejs J, Muller L. Body fat assessment by a new bipedal bioimpedance instrument in normal weight and obese women. *Sb Leuk* 1995; **96**: 249–256.
- 39 Janssen I, Katzmarzyk PT, Ross R. Body mass index, waist circumference, and health risk: evidence in support of current National Institutes of Health guidelines. *Arch Intern Med* 2002; **162**: 2074–2079.
- 40 Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985; **28**: 412–419.
- 41 Wirth A, Krause J. Long-term weight loss with sibutramine: a randomized controlled trial. *JAMA* 2001; **286**: 1331–1339.
- 42 McManus K, Antinoro L, Sacks F. A randomized controlled trial of a moderate-fat, low-energy diet compared with a low fat, low-energy diet for weight loss in overweight adults. *Int J Obes Relat Metab Disord* 2001; **25**: 1503–1511.
- 43 Alper CM, Mattes RD. Effects of chronic peanut consumption on energy balance and hedonics. *Int J Obes Relat Metab Disord* 2002; **26**: 1129–1137.
- 44 Sabate J. *Nuts and body weight: a negative interaction?* Paper presented at 4th International Congress on Vegetarian Nutrition, Loma Linda University, CA, 2002.
- 45 Golay A, Eigenheer C, Morel Y, Kujawski P, Lehmann T, de Tonnac N. Weight-loss with low or high carbohydrate diet? *Int J Obes Relat Metab Disord* 1996; **20**: 1067–1072.
- 46 Rocca AS, LaGreca J, Kalitsky J, Brubaker PL. Monounsaturated fatty acid diets improve glycemic tolerance through increased secretion of glucagon-like peptide-1. *Endocrinology* 2001; **142**: 1148–1155.
- 47 Perfetti R, Brown TA, Velikina R, Busselen S. Control of glucose homeostasis by incretin hormones. *Diabetes Technol Ther* 1999; **1**: 297–305.
- 48 Martens FM, Visseren FL, Lemay J, de Koning EJ, Rabelink TJ. Metabolic and additional vascular effects of thiazolidinediones. *Drugs* 2002; **62**: 1463–1480.
- 49 Taskinen MR, Nikkila EA. Effects of caloric restriction on lipid metabolism in man: changes of tissue lipoprotein lipase activities and of serum lipoproteins. *Atherosclerosis* 1979; **32**: 289–299.
- 50 Abbey M, Noakes M, Belling GB, Nestel PJ. Partial replacement of saturated fatty acids with almonds or walnuts lowers total plasma cholesterol and low-density-lipoprotein cholesterol. *Am J Clin Nutr* 1994; **59**: 995–999.
- 51 Sabaté J, Haddad E, Tanzman, Jambazian P, Rajaram S. Serum lipid response to the graduated enrichment of a Step I diet with almonds: a randomized feeding trial. *Am J Clin Nutr* 2003; **97**: 1379–1384.
- 52 Dattilo AM, Kris-Etherton PM. Effects of weight reduction on blood lipids and lipoproteins: a meta-analysis. *Am J Clin Nutr* 1992; **56**: 320–328.
- 53 Anderson KM, Wilson PW, Odell PM, Kannel WB. An updated coronary risk profile. A statement for health professionals. *Circulation* 1991; **83**: 356–362.
- 54 Fraser GE, Sabate J, Beeson WL, Strahan TM. A possible protective effect of nut consumption on risk of coronary heart disease. The Adventist Health Study. *Arch Intern Med* 1992; **152**: 1416–1424.
- 55 Hu FB, Stampfer MJ, Manson JE, Rimm EB, Colditz GA, Rosner BA, Speizer FE, Hennekens CH, Willett WC. Frequent nut consumption and risk of coronary heart disease in women: prospective cohort study. *BMJ* 1998; **317**: 1341–1345.