

Effects of fresh mango consumption on cardiometabolic risk factors in overweight and obese adults

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KEYWORDS

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Abstract *Background & aims:* In vitro and animal studies show antidiabetic, anti-inflammatory, and cardioprotective properties of mangos. The objective of this study was to examine the effects of fresh mango consumption compared to an isocaloric control snack on body weight, glucose, insulin, lipid profiles, liver function enzymes, inflammation, and antioxidant activity in overweight and obese adults (BMI ≥ 26 kg/m²).

Methods and results: In a crossover design, 27 participants consumed 100 kcal/d of fresh mangos or isocaloric low-fat cookies daily for 12 weeks each, separated by a four-week washout period. Blood glucose, C-reactive protein (CRP), and aspartate transaminase activity significantly decreased while total antioxidant capacity significantly increased following mango consumption. There were no significant changes in body weight, body fat %, blood pressure, insulin, or lipid profile following mango consumption. Cookie consumption significantly increased body weight, insulin, CRP, and triglycerides.

Conclusion: These results suggest that relative to the control snack, mangos may improve certain risk factors associated with overweight and obesity including improved glycemic control and reduced inflammation.

Clinical trials register: NCT03957928.

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Introduction

The prevalence of overweight and obesity has been increasing in the United States since 1980 [1]. The 2015–2016 National Health and Nutrition Examination

Survey (NHANES) reported that over two-thirds of American men and women were overweight or obese [2]. Excess adiposity, particularly visceral fat, is a known risk factor for chronic inflammation, type 2 diabetes mellitus (T2DM), cardiovascular diseases (CVD), and premature mortality

Abbreviations: ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; BIA, bioelectrical impedance; BMI, body mass index; CK, creatine kinase; CVD, cardiovascular disease; DEXA, dual-energy x-ray absorptiometry; γ -GT, gamma-glutamyl transferase; HbA1c, hemoglobin A1c; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, Homeostasis Model of Assessment-Insulin Resistance; LDH, lactate dehydrogenase; LDL-C, low-density lipoprotein cholesterol; LFC, low-fat cookies; NAFLD, non-alcoholic fatty liver disease; PAR-Q, Physical Activity Recall Questionnaire; ROS, reactive oxygen species; TAC, total antioxidant capacity; TC, total cholesterol; TG, triglycerides; T2DM, type 2 diabetes mellitus.

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[3–7]. Many studies have shown the inverse relationship between diet quality and risk of obesity and chronic diseases [8,9]. Therefore, as overweight and obesity continue to rise, interventions aimed at improving overall diet quality are warranted as a strategy to reduce chronic disease risk factors associated with obesity.

Snacking has become ubiquitous in the United States with up to 97% of adults consuming snacks which contribute up to 24% of daily energy intake [10]. Because daily snacking is common, dietary interventions should target the addition of healthy snack choices to improve diet quality. While some studies have shown that snacking can increase total energy intake and lead to weight gain, other studies have found that in general snacking improves overall diet quality [11–14]. For example, the addition of certain foods such as fruits and vegetables has been associated with weight loss likely due to their high fiber and water content which contribute to satiety while maintaining a lower energy density [15,9]. Furthermore, fruits contain many vitamins, minerals, and phytochemicals that may help to prevent various diseases [16,17]. The global burden of disease study found that the number one risk factor for death in the United States was suboptimal diet with one of the most important dietary risk factors being not eating enough fruits – responsible for an estimated two million deaths per year globally [18].

Mangos (*Mangifera indica* L.) may offer unique health promoting properties beyond their vitamin, mineral, and fiber content. Mangos contain many bioactive compounds including mangiferin, gallic acid, gallotannins, quercetin, isoquercetin, ellagic acid, and β -glucogallin [19,20]. Several *in vitro* and animal model studies have shown anti-inflammatory, antioxidant, anti-obesity, and cardioprotective effects of mangos using extracts from the leaves, seed, peel, and bark of the mango [21–24]. These results highlight the potential of mangos as a functional food and have led to an interest in studies examining the effects of mango consumption on various chronic disease risk factors in humans. Some studies of freeze-dried mango (10 g) consumption have shown benefits for fasting blood glucose [25] with no effects on lipid profile or inflammatory markers [26]. While others have shown reductions in certain pro-inflammatory cytokines following 200–400 g of mango pulp consumption for 6 or 8 weeks [27,28]. Due to the mixed results and lack of a control in many of the previous studies, long-term studies using a control group are warranted to examine the metabolic effects of fresh mango consumption, which is how people most often consume mangos.

The objective of our study was to examine the effects of daily fresh mango consumption over 12 weeks on body weight, body fat percentage, glucose, insulin, lipid profile, liver function enzymes, and inflammation in healthy overweight and obese adults compared to an isocaloric snack of low-fat cookies (LFC). The hypotheses were that one cup (166 g) of fresh mango consumption daily would reduce body weight and improve risk factors for CVD compared to an isocaloric LFC snack.

Methods

Study population

A total of 27 subjects (16 males and 11 females) participated in this study. Participants were recruited from San Diego, California from flyers posted throughout the San Diego community. Participants were healthy adults between the ages of 18–55 years with a body mass index (BMI) of 26 kg/m² or higher. Exclusion criteria included those with a mango or gluten allergy and any known medical condition resulting in metabolic disorders or chronic inflammation such as diabetes or cardiovascular diseases which was confirmed with a medical history form and physical activity readiness questionnaire prior to participation. Participants were also excluded if they were smokers, pregnant, lactating, or taking any prescription level dietary supplements. Participants taking nonprescription over the counter dietary supplements such as multivitamins were included and asked to maintain their supplementation regimen for the duration of the study. Female participants must have regular menstrual cycles and began their lab visits 3–11 days after the initiation of their menstrual cycle to control for fluctuations in hormones that could influence blood biomarkers. The study protocol was approved by San Diego State University's Institutional Review Board (IRB) Committee with all participants providing informed written consent prior to beginning the study. The trial was registered at clinicaltrials.gov (NCT03957928).

Study design

Utilizing a crossover design, participants were randomly assigned to two 12-week dietary intervention periods separated by a four-week washout period in between trials. Subjects were randomized using a block size of five with the first five subjects assigned to start with the mango intervention and the next five with LFC alternating until reaching the desired participation. Study visits took place at the laboratory at baseline, week 4, and week 12 for each intervention arm. All lab visits were scheduled in the morning following an overnight fast of at least 10 h. For the baseline and weeks 4 and 12 lab visits, blood samples were collected. Blood samples were centrifuged at 1200×g for 10 min at 4 °C and serum stored at –80 °C until analyzed.

During the interventions, participants consumed approximately 100 Kcal of fresh mangos (166 g, 1 cup, Tommy Atkins, Kent, or Haden cultivars) or low-fat Nilla wafer cookies (24 g, 6.5 cookies, Nabisco, East Hanover, NJ) daily for 12 weeks. The mangos contained 25 g carbohydrates (22.3 g sugar and 2.6 g dietary fiber), 1.35 g protein, and 0.6 g total fat (0.15 g saturated, 0.12 g polyunsaturated, and 0.23 g monounsaturated fat). The LFCs contained 20 g carbohydrates (10 g sugar and 0 g fiber), 0.8 g protein, and 1.3 g total fat (0 g unsaturated, 0.4 g polyunsaturated, and 0 g monounsaturated fat). The 166 g serving of mangos also provided some additional nutrients not found in the LFCs including 88.8 µg vitamin A, 1062.4 µg beta carotene,

60 mg vitamin C, 1.49 µg vitamin E, 6.97 µg vitamin K, and 71.3 µg folate.

Snacks were pre-portioned and were provided in single serving zip lock bags throughout the study. Participants were instructed to consume their snack on its own without other foods or beverages and in one sitting to replicate a typical snack eaten. No specific dietary instructions were given prior to the first intervention. Although mangos are a commonly consumed fruit worldwide [29], it is unlikely many mangos were consumed during the initial lead in period. Compared to other fruits, mangos are not among the most commonly consumed fruits in the US [30] which was supported with the dietary records of the participants. Participants were instructed to not consume mangos during the cookie and washout period. Other than the provided snacks, participants were also instructed to maintain their usual diet and activity level throughout the course of the study. Participants were reminded to consume their daily snack throughout the study at each lab visit and in between visits via email or text reminders.

Diet intake was measured by trained staff using 24-hr dietary recalls for the two days prior to each laboratory visit at baseline, week 4, and week 12. ESHA Research Food Processor Nutrition Analysis program (ESHA, Salem, OR) was used to analyze macro and micronutrient intakes of the diets. Physical activity levels were measured for the previous 7 days at each lab visit using a validated Physical Activity Recall Questionnaire (PAR-Q) [31]. Diet and physical activity data were used to assess groups at baseline and monitor compliance.

Anthropometrical measurement

Participants were asked to refrain from caffeine, alcohol, and exercise during the 24 h prior to each lab visit. Height and weight were measured using a mechanical beam scale with a built-in stadiometer (Detecto, Webb City, MO). Body fat was assessed during each visit by a handheld bioelectrical impedance (BIA; Model HBF-306C, Omron, Lake Forest, IL), BodPod (Model A-661-230-023, Cosmed, Concord, CA), and dual-energy x-ray absorptiometry (DEXA, GE Healthcare Lunar Prodigy, Madison, WI). In addition to total body fat, DEXA was used to determine android and gynoid fat percentage. The regions of interest (ROI) were automatically determined by the enCORE software from the manufacturer. The android ROI included a lower boundary at the top of the pelvis and an upper boundary by 20% of the distance between pelvis and neck cuts. The gynoid ROI included an upper boundary below the pelvis cut line by 1.5 times the height of the android ROI and gynoid ROI height was equal to two times the height of the android ROI. Waist and hip circumferences along with blood pressure (Model Bp710N, Omron, Lake Forest, IL) were also measured at each lab visit.

Biochemical analysis

Serum glucose was measured using a colorimetric assay kit following the manufacturer's instructions (EKF Diagnostics

Inc., Cardiff, UK). Insulin was measured using a sandwich type enzyme-linked immunosorbent assay (ELISA) kit (ALPCO, Salem, NH). Adiponectin was measured using a Human Acrp30 ELISA kit (Ray Biotech, Norcross, GA). Glycated hemoglobin A1c (HbA1c) was measured from a 5 µL fingerstick blood sample using a PTS Diagnostics A1CNow + system (Polymer Technology Systems, Inc. Whitestown, IN).

Lipid profile including triglycerides (TG), total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C) were measured using EKF lipid reagent kits (EKF Diagnostics Inc., Cardiff, UK). Low-density lipoprotein cholesterol (LDL-C) was calculated using the formula: $LDL-C = TC - (HDL-C) - (TG/5)$ [32]. Liver function enzymes including aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), lactate dehydrogenase (LDH), gamma-glutamyl transferase (γ-GT), and creatine kinase (CK) were measured using EKF assay kits (EKF Diagnostics Inc., Cardiff, UK).

Serum CRP was measured using a CRP ELISA kit (Immunodiagnostic, Bensheim, Germany). A peroxidase-labeled detection antibody was used followed by TMB substrate. An acid stopping solution was added and the absorbance was read at 450 nm.

Total antioxidant capacity (TAC) was measured using an antioxidant assay kit (Cayman Chemical, Ann Arbor, MI). The antioxidants in the sample inhibit the oxidation of ABTS (2,2'-azino-di-[3-ethylbenzthiazoline sulphonate]) to $ABTS^{•+}$ by metmyoglobin. The amount of $ABTS^{•+}$ produced was quantified as Trolox equivalents.

Statistical analysis

Sample size was calculated based on the freeze dried mango supplementation study at 80% power and an alpha-level of 0.05 with 20% attrition [25,33]. The data were analyzed by a 2 (trial) x 3 (time) repeated measures analysis of variance (ANOVA) using SPSS version 26 (IBM, Armonk, NY) to examine the effects of mango and LFC consumption on each of the dependent variables over time as well as any significant interaction between snack type and time. For any significant interaction or main effect, paired t-tests were used for post-hoc analysis. Baseline differences between the trials were tested using paired t-tests. If basal values were significantly different following paired t-tests, analysis of covariance (ANCOVA) follow ups were going to be performed using baseline as a covariate. However, no significant differences were found between the trials at baseline regarding the variables so baseline adjusted ANCOVA follow ups were not performed. All data are presented as mean ± standard deviation with a p-value ≤ 0.05 considered statistically significant.

To examine if responses differed with the degree of overweight and obesity, ANCOVA using BMI as an adjustment variable was performed. Adjusted p-values were similar to the repeated measures ANOVA results for most outcome variables and if not, BMI as a covariate itself was not significant. Therefore, only the p-values for repeated measures ANOVAs were included in the results section.

Results

Participants and baseline characteristics

A total of 36 participants were eligible to participate in this study after screening. Four participants could not complete the study due to scheduling conflicts or personal reasons. Five participants were not able to complete the second trial due to safety precautions relating to COVID-19. Therefore, a total of 27 participants (16 males, 11 females) completed this study. The mean age of the participants was 26.0 ± 8.1 years. The mean height was 172.4 ± 8.4 cm. The mean BMI of all participants at baseline was 31.8 ± 4.1 kg/m². Of the BMI categories, 13 participants were classified in the overweight category (25–29.9 kg/m²), 9 obese grade I (30–34.9 kg/m²), 3 obese grade II (35–39.9 kg/m²), and 2 obese grade III (40 kg/m² or higher).

Anthropometrics, blood pressure, diet and physical activity levels

Results for anthropometric measurements and blood pressure can be found in Table 1. A main effect of time was detected for increasing body weight and BMI ($p < 0.05$), which was accounted for by an increase during the low-fat cookie trial only. There were no significant differences for systolic blood pressure (SBP), diastolic blood pressure (DBP), waist circumference, hip circumference, or waist-to-hip ratio. No significant differences were found for body fat percentage across DEXA, BIA, and BodPod measurements; android or gynoid fat percentage; and android-gynoid percent fat ratio. There were no significant differences in physical activity levels or diet intake for total Kcal, fat, protein, fiber, and carbohydrate at baseline, week 4, or week 12. Energy and nutrient intake data can be found in Table 2. The snack serving size of 100 Kcal was achievable with diet history indicating high adherence to the protocol.

Glucose, insulin, adiponectin, and hemoglobin A1c

There was a significant interaction for serum glucose levels ($p = 0.004$) (Fig. 1A), with glucose concentrations dropping from baseline to 4 weeks and remaining lower through 12 weeks during the mango intervention, while no change was detected during the LFC intervention. In addition, there was a significant interaction for serum insulin levels ($p = 0.041$) (Fig. 1B) with no significant change over time points during the mango intervention and a significant increase compared to baseline at both the 4-week and 12-week time points for the LFC intervention. Although it was not statistically significant there was a trend of interaction for adiponectin ($p = 0.063$) (Fig. 1C). Serum adiponectin levels showed trends of increasing at the end of 12 weeks following the mango intervention and decreasing following the LFC intervention. HbA1c did not change during the study (Mangos $5.21 \pm 0.31\%$ at baseline and $5.29 \pm 0.34\%$ at week 12 vs LFC $5.26 \pm 0.33\%$ at baseline and $5.24 \pm 0.32\%$ at week 12).

Lipid profile

Lipid profile results are presented in Fig. 2. Results for triglycerides revealed a significant interaction ($p = 0.043$). LFC consumption significantly increased triglyceride levels after 12 weeks compared to mangos. There were no significant differences for TC or HDL-C. A significant main effect for time was found for LDL-C ($p = 0.016$). During the mango intervention, LDL-C significantly decreased at 4 weeks however levels were not significantly different than baseline by week 12.

Liver function enzymes

Liver function enzymes are presented in Table 3. A significant interaction was found for AST concentrations ($p = 0.041$). AST concentrations significantly decreased at week 12 following mango consumption, and no significant

Table 1 Anthropometric and blood pressure measurements at baseline, week 4, and week 12 during mango and low-fat cookie consumption.

Measurements	Mangos (n = 27)			LFC (n = 27)		
	Baseline	Week 4	Week 12	Baseline	Week 4	Week 12
Body weight (kg)	94.2 ± 14.7^a	94.3 ± 14.4^a	94.6 ± 13.9^a	94.8 ± 14.5^a	95.4 ± 14.4^{ab}	95.7 ± 14.9^b
BMI (kg/m ²)	31.6 ± 4.1^a	31.7 ± 4.0^a	31.8 ± 4.0^a	31.9 ± 4.1^{ab}	32.1 ± 4.1^b	32.2 ± 4.2^b
SBP (mmHg)	120.4 ± 10.1	120.9 ± 12.5	122.9 ± 12.2	119.0 ± 14.0	121.4 ± 13.6	121.1 ± 12.0
DBP (mmHg)	86.9 ± 19.8	82.8 ± 10.6	83.6 ± 8.4	83.6 ± 8.4	81.7 ± 9.8	83.1 ± 8.0
Waist (cm)	98.1 ± 10.8	98.5 ± 11.2	98.9 ± 11.9	99.1 ± 10.4	99.3 ± 9.7	99.8 ± 10.8
Hip (cm)	114.6 ± 8.8	114.8 ± 8.6	115.1 ± 8.4	115.1 ± 9.3	115.0 ± 8.6	115.1 ± 8.6
W/H ratio	0.86 ± 0.07	0.86 ± 0.07	0.86 ± 0.07	0.86 ± 0.06	0.86 ± 0.06	0.87 ± 0.05
Body fat (%) DEXA	39.9 ± 9.1	40.3 ± 9.1	40.6 ± 9.0	40.4 ± 9.1	40.6 ± 8.9	40.7 ± 8.7
Android fat (%) DEXA	49.1 ± 8.3	49.5 ± 8.1	49.6 ± 7.5	49.7 ± 8.0	49.9 ± 7.5	50.1 ± 7.8
Gynoid fat (%) DEXA	44.1 ± 9.2	44.3 ± 9.2	44.4 ± 9.3	44.2 ± 9.6	44.5 ± 9.5	44.3 ± 9.3
A/G ratio	1.17 ± 0.17	1.17 ± 0.17	1.17 ± 0.18	1.18 ± 0.19	1.18 ± 0.19	1.18 ± 0.18
Body fat (%) BIA	30.5 ± 6.5	29.7 ± 6.7	30.6 ± 5.7	30.0 ± 6.4	30.9 ± 6.6	30.8 ± 6.5
Body fat (%) BodPod	28.5 ± 11.5	28.9 ± 11.3	28.2 ± 11.2	29.7 ± 11.5	28.7 ± 12.1	29.4 ± 11.9

Data are expressed as means $\pm$ SDs. N = 27. Data within rows with different superscript letters are statistically different ($p \leq 0.05$). Data within rows without superscripts were not significantly different. BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; W/H: waist to hip ratio; DEXA: dual energy X-ray absorptiometry; A/G: android/gynoid ratio; BIA: bioelectrical impedance analysis.

Table 2 Energy and nutrient intakes at baseline, week 4, and week 12 in the mango and low-fat cookie intervention.

Nutrients	Mangos (n = 27)			LFC (n = 27)		
	Baseline	Week 4	Week 12	Baseline	Week 4	Week 12
Energy (Kcal/d)	2134 ± 714	2259 ± 1006	2293 ± 851	2208 ± 680	2480 ± 2197	2356 ± 918
Protein (g/d)	88.5 ± 39.6	93.3 ± 58.9	92.5 ± 35.3	89.7 ± 38.9	84.4 ± 33.6	102.1 ± 72.2
Total fat (g/d)	84.3 ± 37.3	93.3 ± 41.1	92.2 ± 37.6	88.5 ± 30.0	94.0 ± 63.8	91.9 ± 51.5
SFA (g/d)	24.8 ± 10.5	30.5 ± 14.8	30.5 ± 11.4	30.0 ± 12.8	28.4 ± 13.9	27.0 ± 12.2
MUFA (g/d)	14.3 ± 15.2	17.3 ± 13.8	14.8 ± 11.9	13.4 ± 8.8	12.1 ± 9.4	15.2 ± 17.0
PUFA (g/d)	7.5 ± 6.6	10.7 ± 12.4	8.8 ± 8.4	6.5 ± 3.8	12.2 ± 33.3	7.7 ± 7.1
Total fiber (g/d)	17.8 ± 8.3	22.0 ± 11.5	20.5 ± 10.3	15.9 ± 8.1	15.3 ± 9.5	17.9 ± 8.8

Data are expressed as means ± SDs. There were no significant differences between nutrient intakes between the trials over the time. SFA: saturated fatty acids; MUFA: monounsaturated fatty acids; PUFA: polyunsaturated fatty acids.

differences were found between baseline and week 12 following LFC consumption. No significant changes were found for ALT, ALP, CK, LDH, or γ -GT.

C-reactive protein

Results revealed a significant interaction for serum CRP levels following the interventions ($p = 0.001$) (Fig. 3). Serum CRP decreased from baseline to weeks 4 and 12 during the mango intervention and increased from baseline to week 12 during the LFC intervention.

Total antioxidant capacity

For TAC, there was a main effect for time ($p = 0.002$) (Fig. 4). Serum TAC significantly increased from baseline to week 4 during both the mango and LFC interventions. TAC remained

elevated during the mango intervention through week 12 but decreased slightly and was not significantly different than baseline at the end of 12 weeks for the LFC intervention.

Discussion

Mangos are among the most commonly consumed fruits worldwide and contain many antioxidants and other bioactive compounds such as mangiferin that may offer unique health benefits [29,34]. This study examined the effects of daily fresh mango consumption compared to an isocaloric amount of LFC on glucose, insulin, lipid profiles, liver function, and inflammation in healthy overweight and obese adults. The results of this study indicated that mangos improved glycemic control and reduced inflammation suggesting that they are a healthful snack alternative to a commonly consumed processed snack food.

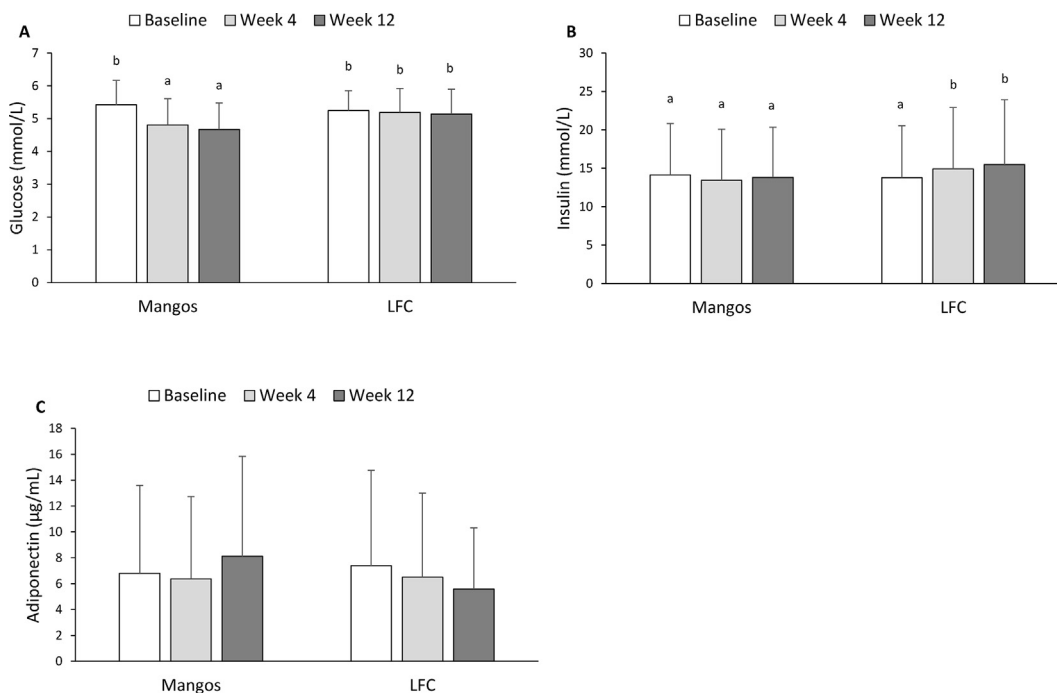


Figure 1 (A) Effects of mangos and LFC (low-fat cookies) on fasting blood glucose. (B) Effects of mangos and LFC on fasting insulin levels. (C) Effects of mangos and LFC on fasting adiponectin levels. Data are presented as means ± SDs (n = 27). Within a variable, values with different letters are statistically different at $p \leq 0.05$.

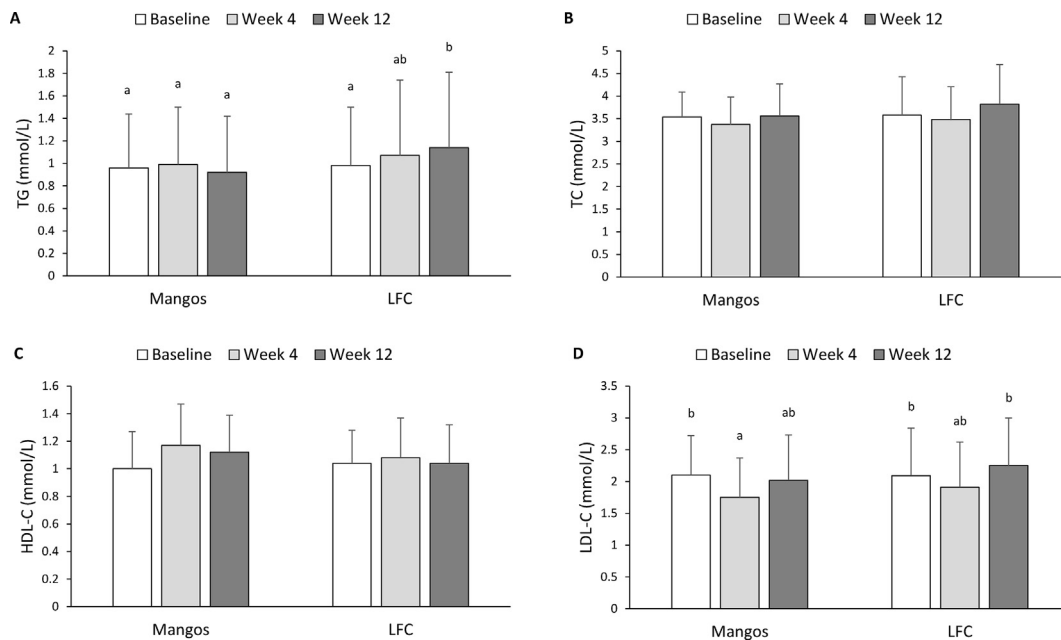


Figure 2 Effects of mangos and LFC (low-fat cookies) on serum concentrations of (A) triglycerides (TG), (B) total cholesterol (TC), (C) high-density lipoprotein cholesterol (HDL-C), and (D) low-density lipoprotein cholesterol (LDL-C) at baseline, week 4, and week 12. Data are presented as means $\pm$ SDs ($n = 27$). Within a variable, values with different superscript letters are statistically different at $p \leq 0.05$.

Research has shown that as BMI increases so does the risk for cardiovascular morbidity and mortality [35]. In this study, the only significant increase was in body weight at the end of 12 weeks following LFC consumption. This increase was small, yet even small increases warrant further investigation as weight gain has been shown to occur gradually over time [9]. Although the snacks were isocaloric, the mangos may have contributed to less weight gain compared to the LFCs due to their fiber and water content. Increasing fiber and water ingestion through food consumption may promote greater satiety while lowering the energy density of the diet compared to a processed snack [36]. Fang et al. similarly found no changes in body weight or composition in obese adults consuming up to 400 g (240 Kcal) of mango pulp daily [27]. This is likely due to the energy content of participants' diets, which remained constant over the 6-week trial suggesting that natural compensatory behavior as a result of the additional Kcals of the daily mango consumption. This adds support to

previous research demonstrating that the addition of whole fruits to the diet does not negatively impact body weight [15,9].

The reductions in fasting blood glucose seen in this study were similar to previous research in obese adults consuming 10 g of freeze-dried mango daily over 12 weeks [25]. Interestingly, a much larger dose of 400 g of mango pulp resulted in no change in fasting blood glucose after 6 weeks [27]. Despite the larger dose, the lack of change may have been due to the shorter duration of that study, which may not have been long enough to engender changes in the obese population. Although the mangos contained more than twice as much sugar as the LFC (22.3 g compared to 10 g), the sugar in mangos is accompanied by both fiber and polyphenols which may both independently contribute to glucose control. Fiber, particularly soluble fiber, has been shown to improve glycemic control by increasing viscosity in the gastrointestinal tract thereby slowing the absorption of carbohydrates in the small

Table 3 Liver function enzyme measurements at baseline, week 4, and week 12 during mango and low-fat cookie consumption.

Measurements	Mangos ($n = 27$)			LFC ($n = 27$)		
	Baseline	Week 4	Week 12	Baseline	Week 4	Week 12
AST (U/L)	20.2 $\pm$ 8.9 ^a	17.2 $\pm$ 8.4 ^{ab}	15.9 $\pm$ 4.9 ^b	20.7 $\pm$ 7.6 ^a	18.6 $\pm$ 5.3 ^a	21.0 $\pm$ 6.5 ^a
ALT (U/L)	22.4 $\pm$ 10.7	20.6 $\pm$ 10.2	21.6 $\pm$ 9.4	22.0 $\pm$ 8.0	21.3 $\pm$ 7.5	24.4 $\pm$ 8.1
ALP (U/L)	60.8 $\pm$ 21.6	64.7 $\pm$ 14.1	58.3 $\pm$ 16.3	61.8 $\pm$ 15.2	63.6 $\pm$ 15.1	57.7 $\pm$ 18.1
CK (U/L)	55.4 $\pm$ 44.4	52.2 $\pm$ 40.3	59.4 $\pm$ 57.9	51.9 $\pm$ 44.0	51.2 $\pm$ 57.1	58.9 $\pm$ 49.8
LDH (U/L)	123.5 $\pm$ 24.8	124.3 $\pm$ 20.1	120.1 $\pm$ 22.9	132.8 $\pm$ 21.3	121.3 $\pm$ 20.7	123.1 $\pm$ 23.6
γ GT (U/L)	15.6 $\pm$ 10.6	15.8 $\pm$ 13.2	14.0 $\pm$ 7.9	15.9 $\pm$ 13.6	14.5 $\pm$ 9.4	15.0 $\pm$ 10.8

Data are expressed as means $\pm$ SDs. $N = 27$. Data within rows with different superscript letters are statistically different ($p \leq 0.05$). Data within rows without superscripts were not significantly different. AST: aspartate transaminase; ALT: alanine transaminase; ALP: alkaline phosphatase; CK: creatine kinase; LDH: lactate dehydrogenase; γ GT: gamma-glutamyl transferase.

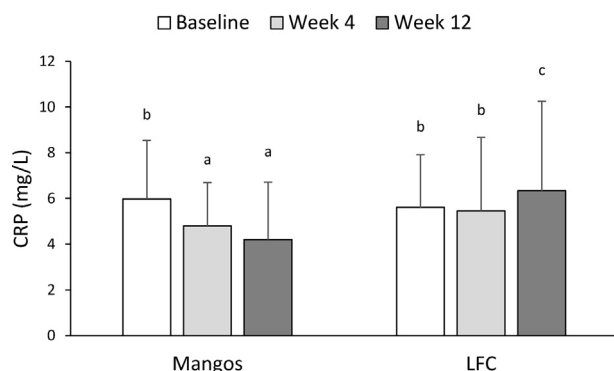


Figure 3 Effects of mangos and LFC (low-fat cookies) on C-reactive protein (CRP) levels at baseline, week 4, and week 12. Data are presented as means $\pm$ SDs ($n = 27$). Within a variable, values with different letters are statistically different at $p \leq 0.05$.

intestine [37]. In addition, research has shown that certain fruit polyphenols can inhibit intestinal uptake and transport of glucose independent of fiber [38,39]. One of the most studied polyphenols in mangos is mangiferin, a polyphenolic antioxidant which in extract form has been shown to lower fasting plasma glucose levels in animal models [40]. The reduction in fasting blood glucose suggests that adding mango to one's diet may benefit people with overweight and obesity since they are at increased risk of developing T2DM.

The effects of mango consumption on measures of insulin sensitivity in humans, which may be a better predictor of long-term glycemic control, is less clear. Freeze-dried mango consumption has been shown to lower insulin resistance in mice fed a high fat diet as measured by HOMA-IR similar to that of the hypoglycemic drug, rosiglitazone [41]. However, human trials have not seen the same degree of effects on measures of insulin sensitivity, with one study finding a nonsignificant trend towards reductions in HbA1c [25,27]. In the present study, there was a significant increase in fasting insulin during the LFC intervention with no change during the mango intervention. Higher fasting insulin levels have been associated with increased likelihood of identifying prediabetes in addition to other

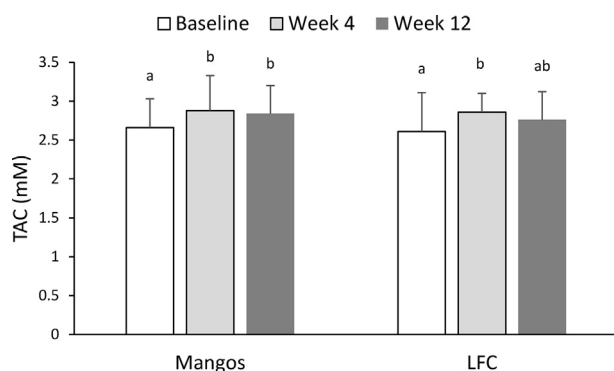


Figure 4 Effects of mangos and LFC (low-fat cookies) on total antioxidant capacity (TAC) at baseline, week 4, and week 12. Data are presented as means $\pm$ SDs ($n = 27$). Within a variable, values with different letters are statistically different at $p \leq 0.05$.

cardiometabolic risk factors [42,43]. The participants in the current study were all metabolically healthy; future studies that examine the effects of mango consumption in those already with insulin resistance may reveal different results.

Adiponectin is an adipokine released by adipose tissue known to exhibit antihyperglycemic effects by increasing basal glucose uptake and enhancing insulin through AMP kinase (AMPK) activation [44]. Adiponectin concentrations have been demonstrated to decrease with obesity and increase following weight loss [45]. Although not reaching statistical significance, there was a trend towards increased adiponectin concentrations following mango consumption and decreased concentrations following LFC consumption. Adiponectin levels trended favorably following mango consumption despite no reductions in body weight indicating a potential mechanism for the observed improvements in blood glucose.

Although there were no changes in lipid profile following mango consumption, serum TG levels increased after 12 weeks of LFC consumption suggesting that mangos were a better alternative for maintaining lipid profiles compared to the control snack. Mangiferin supplementation (150 mg/day) has been previously shown to reduce TG levels in subjects with overweight and hyperlipidemia [46]. However, other studies adding the consumption of freeze dried and mango pulp in adults with obesity found no changes in lipid profiles [26,27]. One study comparing 200 g of whole (remained unsliced until use) versus fresh cut mangos (pre sliced and stored for 10 days) in normolipidemic adults found significantly lowered fasting plasma TGs after 30 days for both whole and fresh cut mangos [47]. One reason this study may have found a reduction in TG is that the participants all had a BMI less than 26 kg/m². Previous research has demonstrated that the bioavailability of mango polyphenols may be reduced with increasing BMI [27]. This may in part explain why studies in populations with overweight/obesity have not seen the favorable effects on lipid profile one would expect based on studies in animal models [23,24].

It is well established that obesity increases the risk of developing nonalcoholic fatty liver disease (NAFLD) which has become one of the most common causes of chronic liver disease in the United States [48,49]. Some markers for liver function have previously been shown to improve with mango leaf and mango powder supplementation in animal models [50,51]. The present study was one of the first that examined the effects of fresh mango consumption on liver function enzymes in humans. A decrease in AST was observed following mango consumption. Although increased levels of AST are associated with both obesity and increased risk for developing NAFLD, other liver function enzymes did not change with mango consumption suggesting minimal effects on liver health from this study [52]. To confirm these results, future studies should examine the effects of long-term mango consumption on liver function in humans.

Mangos are a rich source of antioxidants such as xanthones, beta-carotene, and ascorbic acid, which may help to reduce the damage to proteins, lipids, and DNA caused by

reactive oxygen species (ROS) [53,54]. Some studies adding mangos to the diet of healthy humans and those with inflammatory bowel disease have demonstrated reductions in certain inflammatory cytokines [27,28]. Other studies have found no changes in inflammatory markers (IL-6 and TNF- α) including during the post-prandial period for the antioxidant enzymes superoxide dismutase, glutathione peroxidase, and catalase [26,55]. In our study, TAC increased at week 4 for both the mango and LFC intervention but only during mango consumption did TAC remain significantly higher after 12 weeks. Although the measurement of TAC has its limitations, this measurement of overall antioxidant capacity considers the cumulative effect of all antioxidants present, which may provide a better overview of the potential to protect against ROS than any single antioxidant measurement [56]. One of the antioxidants present in mangos is mangiferin, which may reduce oxidative stress through a variety of pathways including prevention of increased levels of glucocorticoids, interleukin-1 β , lipid peroxidation, and other pro-inflammatory mediators [57]. Furthermore, CRP levels decreased during the mango intervention and increased during the LFC phase. This further supports the findings that mangos provided more antioxidant protection to reduce inflammation compared to the LFCs. Future studies should additionally measure high sensitivity CRP as it may better predict chronic inflammation and coronary artery disease risk [58].

While this was one of the first mango studies in humans to include a control snack, one limitation is that only one dose of mangos was used so the optimal dose cannot be determined from this study alone. This dosage, however, represents a practical amount for general snack recommendations as 166 g equates to about one cup of mangos or one serving of fruit. Additionally, future studies may choose to include a fiber-matched control snack to separate out the effects of the fiber from other bioactive compounds found in mangos. Since the bioavailability of mango polyphenols may be reduced in persons with obesity [27], future studies would be interesting to measure plasma mango metabolites to monitor absorption. The bioavailability of mango polyphenols also depends upon other factors including cultivar, harvest time, degree of ripeness, food matrix, enzyme activity, and microbiota which should be addressed in future studies [59]. Participants were given reminders about snack consumption throughout the study which was also assessed during the 24-h recalls at each lab visit; however, future studies may wish to more objectively measure compliance for each day of the study. Finally, this study measured the effects of mango consumption in adults without known pre-existing health conditions. Therefore, studies examining the long-term effects of mango consumption in those already with metabolic conditions such as T2DM or dyslipidemia are warranted.

Conclusions

This study was one of the first to examine the effects of fresh mango consumption compared to an isocaloric

control snack in overweight/obese adults. Results suggest that compared to the LFC snack, mangos were a healthier alternative that improved blood glucose control, inflammation, and antioxidant status. Mangos are a widely consumed fruit and should be considered for future research as they contain a variety of bioactive compounds with the potential to improve diet quality and modulate human disease risk factors.

Clinical trial

The study was registered at clinicaltrials.gov (#NCT03957928).

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Author contributions

Martin Rosas Jr.: Formal analysis, investigation, data curation, writing original draft, writing-reviewing and editing, visualization and project administration; **Sherry Pinneo:** Investigation; **Celeste O'Mealy:** Investigation and project administration; **Michelle Tsang:** Investigation; **Changqi Liu:** Conceptualization, methodology and writing-reviewing and editing; **Mark Kern:** Conceptualization, methodology and writing-reviewing and editing; **Shirin Hooshmand:** Conceptualization, methodology and writing-reviewing and editing; **Mee Young Hong:** Conceptualization, methodology, formal analysis, investigation, resources, data curation, writing-reviewing and editing, supervision and funding acquisition.

Declaration of competing interest

The authors declare no conflict of interest.

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