Influence of Mangos on Vascular Function and Platelet Reactivity in Postmenopausal Women

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Abstract

Mangos are rich in mangiferin, a phenolic acid that has multiple bioactive effects. Combined with carotenoids, fiber and other nutrients, mangos may be of benefit to vascular health. This study assessed whether a short-term (14 days) or acute (two hours) intake of mangos can influence: 1) microvascular function and the augmentation index, determined by peripheral arterial tonometry; 2) blood pressure; 3) optical platelet aggregometry, and 4) gut fermentation, determined by breath hydrogen and methane, in healthy adult women.

25 healthy postmenopausal females (BMI 25-40 kg/m^2) were assessed at three study visits. Study visit 1 (SV1) started a run-in period of 14 d during which no mangos were consumed, with baseline and two-hour measures taken. At study visit 2 (SV2), baseline (0 hour) measures were taken, followed by ingestion of 300 gm (two cups) of fresh, frozen mangos, and data were collected two hours later. Participants then consumed 300 g of mangos daily for 14 days, followed by assessment at study visit 3 (SV3), which followed the same protocol as SV2. Breath samples were collected at baseline at each study visit.

A significant interaction between treatment and time (p=0.005) was observed for systolic blood pressure (SBP). At baseline, SBP was not significantly different between study visits, however SBP was significantly lower two hours after mango intake during SV2 and SV3 compared to no mango intake during SV1 (112 ± 9 mmHg SV2 vs. 116 ± 12 SV1, P=0.013; 111 ± 11 mmHg SV3 vs. 116 ± 12 SV1, P=0.003). A significant treatment effect was noted for mean arterial pressure (p=0.04) with mango intake compared to no mango intake (90 ± 7 mmHg SV2 vs. 89 ± 9 SV1, P=0.04; 86 ± 8 mmHg SV3 vs. 89 ± 9 SV1, P=0.005). Pulse pressure was significantly reduced two hours after intake compared to baseline during SV2 (41 ± 7 mmHg baseline vs. 38 ± 5 2 h, P=0.005). Breath methane was significantly reduced in three of six participants that produced methane.

Two cups of mango intake had acute (two hour) beneficial effects on blood pressure in healthy postmenopausal women. A number of women showed favorable changes in breath methane, an indication of the potential influence of mango intake on gut fermentation.

Introduction and project objectives

Cardiovascular disease (CVD) is the leading cause of mortality in the U.S, and aging is a nonmodifiable risk factor for vascular diseases (Koene et al., 2016). For postmenopausal women, this risk is particularly elevated due to the loss of the protective effect of estrogen (Atsma, et al., 2006). Nutrition plays a crucial role in prevention of chronic diseases such as heart disease and an abundant intake of plant-based food is known to lower the risk of CVD (Aune et al., 2017). However, which plant foods confer the most cardioprotective effects is not well understood.

Polyphenolic compounds in fruits and nuts have been the focus of extensive research regarding their potential to reduce risk for a number of chronic diseases. Mangos *(Mangifera Indica L.),* a commonly cultivated fruit worldwide, are rich in polyphenolic compounds such as gallic acid, mangiferin, quercetin glycosides, ferulic acid, and hydroxybenzoic acid (Masibo et al., 2008). Many of those bioactive compounds, especially mangiferin, have been found to have anti-cancer and anti-inflammatory effects in animal and cell models. For instance, mangiferin has been shown to effectively reduce glucose-induced endoplasmic reticulum stress by inhibiting IREα phosphorylation and ROS production in endothelial cells (Song et al., 2015). In mice fed high-fat diets, adding freeze-dried mango to the diet lowered the blood glucose and plasma lipids (Lucas et al., 2011). In isoproterenol-induced cardiotoxic myocardial infarcted rats, mangiferin significantly reduced the cholesterol, triglycerol, free fatty acids levels in serum and heart (Nair & Devi, 2006). Additionally, fermentation from fibers and polyphenols in mango increased the production of anti-cancer short chain fatty acids in mice fed high fat diets (Ojo et al., 2016).

Studies regarding the effects of mango or mango products in humans are rare. One study found that after a 12-week supplementation of freeze-dried mango powder to obese individuals, blood glucose and hip circumference were significantly reduced (Evans et al., 2014), but effects on vascular function are unknown. This information is critical in evaluating the potential benefits of mangos on reducing the risk of CVD, or making claims about the “heart health” benefits of mangos.

The overall objective of this study was to investigate the effects of acute and short-term daily mango intake on markers of vascular function and platelet aggregation. We also assessed production of breath hydrogen and methane, two markers of gut fermentation from sugars and starches.

Materials and methods

Of 213 postmenopausal women (50–70 years of age) who volunteered for the study, 28 met inclusion and exclusion criteria and were enrolled. After qualification, on Study Visit 1 (SV1), the participant arrived at our laboratory in the morning after a 12-hour fast and after following a 24-hour low polyphenol diet. The participant was asked to refrain from vigorous physical activity 24 hours prior to arriving at the laboratory. Procedures were performed at the same time of the day to minimize circadian effects. Anthropometric measures (height, weight and waist circumference), heart rate and blood pressure (BP) were recorded, followed by a 30-minute resting period lying on a bed. A baseline measurement of microvascular function was made by peripheral arterial tonometry (PAT), and blood samples were collected to assess platelet aggregation, complete blood cell count (CBC), high sensitivity C-reactive protein, a comprehensive metabolic panel (CMP) and lipid profiles (LP). A breath sample was collected after the blood collection. Two hours later, a second PAT measurement and blood samples were collected. Water was provided throughout the test period. The participant then followed their normal daily diet but eliminated mango intake for 13 days, after which she returned to the lab for Study visit 2 (SV2), again following a 12-hour fast and 24-hour low polyphenol diet. A PAT measurement and blood sample was collected, after which the participant consumed one portion (two cups) of mango, and two hours later, a second PAT test and blood sample was collected. The participant was given a two-week supply of fresh, frozen mangos and instructed to consume one portion daily while maintaining their normal diet. After two weeks, on Study Visit 3 (SV3), the person was assessed again as described above for SV2.

Compliance was assessed verbally and through self-reported logs, and a 3-day food record (two weekdays and one weekend day) was collected, along with a weekly log book of adverse digestive tract symptoms such as bloating, gas, or cramps.

The portion size of mango was 330 grams (2 cups), which provided an estimated 99 Calories according to the USDA Nutrient Database. With advice from the National Mango Board, a polyphenol-rich variety of mango, Ataulfo, was chosen for the study. A single batch of mangos originated from same orchard and harvested in the same season was used. The mangoes were shipped to the UC Davis Department of Nutrition and allowed to ripen under ambient conditions until they were a light-yellow color with a medium soft texture, at which time they were washed, manually peeled and deseeded, cubed, weighed into daily portions and frozen at -20^{o}C until needed.

The number of participants needed for the study was determined using power calculations from a previous study in our lab assessing the effects of walnuts on vascular function. Assumptions were made that vascular function, as calculated by the reactive hyperemia index (RHI) would have a standard deviation of 0.5, so that a sample size of 20 would be needed to detect differences in RHI measurements of about 0.5 with 80 percent power at a five percent level of significance.

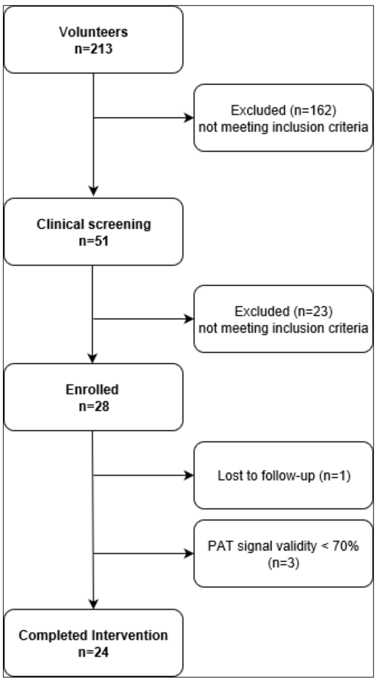
The research protocol was approved by the Institutional Review Board at the University of California, Davis, and registered on clinicaltrials.gov.

Vascular function was assessed using PAT, which measures the change in digital arterial blood volume largely mediated by nitric oxide. Like flow mediated dilation (FMD), PAT is performed under reactive hyperemic conditions and correlates well with FMD. After acclimation to ambient conditions for a minimum of 30 minutes in a supine position, BP was measured on the control arm. Non-invasive, single-use probes were fitted to a finger on each hand, and a baseline amplitude was recorded. Reactive hyperemia was induced by inflating a BP cuff on the test forearm to 60 mmHg above systolic pressure. The cuff pressure was maintained for five minutes, after which cuff pressure was immediately released. Measurements were recorded for both the test arm and the contralateral arm (arm with no occlusion) using the PAT device and final data calculated with the software's automated algorithm, independent of the operator. The software detected pre-occlusion, occlusion, and post-occlusion periods and calculated a RHI as the ratio of the average amplitude of the RHI signal over a one-minute time interval starting one min after cuff deflation, divided by the average amplitude of the RHI signal at 3.5 minutes before cuff inflation. The RHI of the test arm was normalized to the control arm to compensate for potential systemic changes. In addition, the software calculated an augmentation index, which is used as a measure of arterial stiffness.

Platelet aggregation was measured using platelet aggregometry. Platelet rich plasma (PRP) was measured in duplicate using a 2-channel Chrono-Log 700 (Havertown, PA). Platelet aggregation was stimulated with arachidonic acid or collagen and monitored for seven minutes. All plasma was incubated for at least three minutes at 37^{o}C prior with a stirring speed set at 1200 RPM before addition of all agonists.

For breath collection, the participant was asked to perform one short exhalation (about two to three seconds) into a collection bag. The breath sample was analyzed for hydrogen and methane, two gases that are produced by fermentation of carbohydrates (including fiber) in the digestive tract, which may also be influenced by polyphenol content.

Results



Of the 28 women who were enrolled in the study, one dropped out, and insufficient data was collected on three others due to instrumentation errors. Thus, 24 complete records were obtained for the final analysis.

At baseline, SBP was not significantly different between study visits. Remarkably, SBP was significantly lower two hours after mango intake during SV2 compared to baseline (0 hour) values on that day (116 ± 11 mmHg vs. 112 ± 9 mmHg, p=0.004), while no differences were noted between zero and two hours during SV1 or SV3; (Table 1). However, significant reductions in SBP were noted at two hours when comparing the values between SV1 and SV2 (116 ± 12 SV1 vs 112 ± 9 mmHg SV2, P=0.013) and when comparing the two-hour values between SV1 and SV3 (116 ± 12 SV1 vs. 111 ± 11 mmHg SV3, P=0.003).

Consistent with the reductions on SBP noted during SV2 and SV3 compared to SV1, a significant reduction was noted for mean arterial pressure (89 ± 9 SV1 vs 87 ± 6 mmHg SV2, P=0.04), as well as a significant reduction between values for SV3 compared to SV1 (89 ± 9 SV1 vs. 86 ± 8 mmHg SV3, P=0.005).

Also, consistent with the pattern of reduction in SBP at SV2, pulse pressure was significantly reduced at SV2 two hours after mango intake compared baseline (zero hours) values (41 ± 7 mmHg baseline vs. 38 ± 5 at two hours, P=0.005). Pulse pressure was significantly reduced when comparing the two hour values between SV1 and SV2 (41 ± 7 mmHg SV1 vs. 38 ± 5 mmHg at SV2).

Changes in measures of reactive hyperemia (RHI) did not appear to be statistically significant. Since blood pressure is a different vascular response compared to reactive hyperemia, our findings suggest different mechanisms of action for mangos between the two responses. We don't fully understand these differences, and are employing new statistical analyses to further probe this data.

No changes in measures of platelet reactivity were noted. This may be due to the long-term nature of platelet changes, and the two-week intervention was simply not sufficient in length to note changes that have been reported when flavanol-rich supplements are ingested, but not from whole foods.

Breath hydrogen and methane levels were variable. Breath levels reflect the amount of these gases due to microbial fermentation in the intestinal tract. Some people produced hydrogen, some produced methane, some produced both gases and some produced neither. Breath gases are a new outcome measure in nutrition research, and the implications are still not clear, although production of methane is thought to be associated with obesity. The most interesting observation we noted was that six of the 24 participants produced methane, and of these six, three showed a significant reduction, which is considered a favorable outcome.

Further data analysis is ongoing to explore possible vascular and platelet responses that require advanced investigation. Additionally, although not part of the original study proposal, four measures of inflammatory markers, and five markers of platelet function, have been completed, and these data are being analyzed in conjunction with the vascular measures reported above.

Conclusions

Two cups of mango intake had acute (two hour) beneficial effects on systolic blood pressure in healthy postmenopausal women. The favorable changes in systolic blood pressure were generally mirrored by similarly beneficial responses for mean arterial pressure and pulse pressure. A number of women showed favorable changes in breath methane, an indication of the potential influence of mango intake on gut fermentation. Taken as a whole, the results suggest that mango intake, under the conditions tested, can relax blood vessels in as little as two hours after intake. Mangos may be a "heart healthy" fruit that could help reduce the risk of cardiovascular disease. Longer term studies, involving other population groups in addition to healthy, postmenopausal women, are warranted.

Publications and presentations

An abstract of our results was submitted to Nutrition 2018, the annual meeting of the American Society for Nutrition, to be held June 9 to 12, 2018 in Boston (attached). Ms. Xiang Li, the study coordinator and PhD student with Professor Hackman, has also entered the graduate student competition at the meeting.

Following further statistical analysis, we anticipate submission of a manuscript in April 2018. Tentatively, we are targeting the Journal of the American College of Nutrition as the publication, though a final decision has not yet been made in this regard.

We will work closely with the UC Davis Office of Strategic Communications regarding press releases, media interviews, and social media postings. Since ours is the first study to demonstrate favorable vascular effects of mango intake in humans, we are optimistic that attention will be given to our research, and to this fruit, by many sectors of the health professions and general public.

Budget

All funds have been expended in the categories outlined in the original proposal, and modified with the permission of Dr. Ortega.

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