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File: ■ Grapefruit (*Citrus x paradisi*)
■ Weight Loss
■ Obesity

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**RE: Ingestion of a Grapefruit Preload before Meals Improves Weight Loss and
Cardiometabolic Risk in Obese Individuals**

Silver HJ, Dietrich MS, Niswender KD. Effects of grapefruit, grapefruit juice and water preloads on energy balance, weight loss, body composition, and cardiometabolic risk in free-living obese adults. *Nutr Metab (Lond)*. 2011;8(1):8. Doi: 10.1186/1743-7075-8-8.

Eating a low energy density (kilograms per gram of food) diet is an effective weight loss strategy, as it increases satiety while limiting caloric intake. It is particularly effective when the low energy density food is eaten before a meal as a "preload"; however, there is still much discussion over the best form of the preload (solid or liquid). Since the water content of the food is a major determinant of energy density, and fiber is known to increase satiety, the authors hypothesized that fruit may be a good preload candidate food. Grapefruit (*Citrus x paradisi*) was noted for its high water and fiber content, as well as its publicity in the media as a weight loss food and was chosen for assessment. This randomized, open-label, parallel-arm design study sought to test whether grapefruit eaten as a preload would promote weight loss and reduce cardiometabolic risk in obese adults.

The study took place at Vanderbilt University in Tennessee. Subjects (n=95) were obese (body mass index [BMI] 30-39.9 kg/m² and <300 lbs) but otherwise healthy adults, 21-50 years of age. At the enrollment visit, registered dietitians obtained demographic information and diet, weight, BMI, waist and hip circumference, and gastrointestinal health history. Subjects were asked to maintain a stable weight before the first study day and trained to use estimated food portions. Unannounced telephone 24-hour baseline dietary recall surveys were performed twice during the week and once on a weekend.

Following the first clinic visit, subjects entered the caloric restriction phase, which lasted 2 weeks. They were prescribed a diet plan providing a 12.5% calorie restriction compared to each individual's average baseline energy intake. The macronutrient composition complied with the Acceptable Macronutrient Distribution Ranges of 30% fat, 50% carbohydrate, and 20% protein. Subjects were instructed not to consume any grapefruit, grapefruit juice, or dietary supplements for the duration of the phase but were

to consume 3 fruit servings daily. They were also given pedometers to record their steps but were instructed to maintain their usual amount of exercise.

Of the 95 subjects, 85 (64 women, 21 men) complied with the caloric restriction phase, and these were moved into the caloric restriction plus preload phase of 12 weeks. Subjects were randomized into 1 of 3 open groups: 1) the grapefruit group (GF; Florida lot 4281, size 36, 256 g unit weight), eating ½ a grapefruit, 2) the grapefruit juice group (GFJ; unsweetened 100% white GFJ; Ocean Spray; Lakeville-Middleboro, Massachusetts), drinking 127 g, or 3) the water group (Nestlé Pure Life; Greenwich, Connecticut), drinking 127 g. All treatments were consumed 20 minutes before each breakfast, lunch, and dinner meal. The GF and GFJ preloads were matched for energy density by weight, kilocalories, water, and vitamin C contents, but GF provided more fiber and GFJ more flavonoid [measured as naringin] content.

At baseline, week 2 (finish of caloric restriction phase), and week 14 (finish of caloric restriction plus preload phase), subjects were assessed for anthropometric and dietary data and resting energy expenditure (REE). Visual analog scales (VAS) were administered to rate hunger, thirst, satiety (amount that could be consumed), appetite (desire for food), and fullness.

There were no differences in demographics between the treatment groups, and 17 subjects dropped out of the study between weeks 6-9 due to job schedule conflicts and family constraints. Subjects had an average weight loss of 0.99 ± 0.50 kg (2.2 lbs) during the caloric restriction phase. The rate of weight loss increased significantly by 13.3% ($P < 0.0001$) during the caloric restriction plus preload phase for an additional loss of 5.8 ± 3.9 , 5.9 ± 3.6 , and 6.7 ± 3.1 kg (12.8, 13.0, and 14.8 lbs) for GF, GFJ, and water groups, respectively. Weight loss significantly correlated with reduced waist circumferences ($r = 0.37$, $P = 0.004$) of 2.9 ± 4.1 , 5.5 ± 5.7 , and 5.4 ± 4.8 cm, for GF, GFJ, and water groups, respectively, and BMI concurrently decreased significantly.

Average reported total energy intake during the caloric restriction phase decreased by 9% in the GF group, 5% in the GFJ group, and 5% in the water group; however, when preloads were combined with caloric restriction, average dietary energy density decreased by 27.9% in the GF group, 21.6% in the GFJ group, and 20.3% in the water group. Average total energy intake decreased by 21% in the GF group, 29% in the GFJ group, and 28% in the water group. After adjustment for baseline values, between-group differences in dietary energy density and total energy intake were not statistically significant.

There were no significant changes in mean VAS ratings for hunger, thirst, satiety, or fullness, but VAS ratings for appetite significantly decreased in the GFJ group from 80 ± 4 to 58 ± 6 mm ($P = 0.002$). There were no statistically significant differences among groups for respiratory quotient, substrate oxidation rates, REE, or REE adjusted for fat-free mass. Although pedometer counts indicated no difference among groups in steps walked daily, walking exercise capacity significantly improved for all groups with a mean change from 283 ± 3.5 to 269 ± 3.3 seconds ($P < 0.001$).

The mean changes in total cholesterol and low-density lipoprotein cholesterol (LDL-C) did not differ significantly from baseline; however, there was a mean increase in high-density lipoprotein cholesterol (HDL-C) from baseline by 6.2% in the GF group and 8.2% in the GFJ group which differed significantly from the mean decrease of 3.7% in the

water group ($P=0.003$ and $P=0.009$, respectively). There were no significant changes from baseline detected in blood pressure, fasting glucose, insulin, and $HOMA_{IR}$ (homeostasis model assessment of insulin resistance) scores, perhaps a reflection of baseline and study completion values that were within normal ranges.

Overall, the proportion of subjects who met criteria for metabolic syndrome significantly decreased from 27% at baseline to 20% at study completion ($P<0.001$).

In this study, dietary energy density intake declined 20-28% and total energy intake decreased 21-29%, translating into an 8.5-16.5% (~250-500 kcal/d) greater reduction in calories consumed after preloads were incorporated into the restricted calorie meal plan; even so, subjects remained satiated. The authors explained that the subjects not only adjusted the total amount of their food intake to take into account the preloads, but also compensated for the energy content of the preloads by decreasing energy intake from the 3 meals and 3 snacks to achieve an overall reduction in total energy intake. This is in contrast to some basic science models of weight loss that contend that obese individuals would counter weight loss with ingestion of more calories and shows that in practice a preload can be effective and may fundamentally influence mechanisms involved in energy homeostasis.

The 2 forms of grapefruit (solid or liquid) were equally efficacious in weight loss benefit, and even water produced the same weight loss effect, suggesting that simply a preload of weight and volume is the important factor. The grapefruit preloads had the added benefit of increasing HDL-C, reducing cardiometabolic risk, whereas water decreased HDL-C. The authors note that the overall weight loss of 7.1% of initial body weight seen in all groups was clinically meaningful based on the current consensus that 5-10% weight loss decreases cardiometabolic risk.

This study demonstrated the success of using a preload for weight loss and reduction of cardiometabolic risk. This was done without reducing the total amount of food consumed, but by reducing the energy density consumed while being able to maintain satiety and high compliance. The nature of the preload itself can confer additional cardiometabolic benefits. The study has two weaknesses: (1) The use of grapefruit is somewhat problematic, since grapefruit has been shown to contain an enzyme inhibitor that has an effect to reduce metabolic syndrome. It is likely this is the reason seen for the increase in HDL-C not seen in the water group. (2) The second weakness was the use of dietary recall which has been shown in comparison to doubly labeled water to have 50% variability.

—*Risa Schulman, PhD*

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