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Examination of the Antiglycemic Properties of Vinegar in Healthy Adults

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Key Words
Acetic acid · Diabetes · Postprandial glycemia · Vinegar

Abstract
Background: Vinegar reduces postprandial glycemia (PPG) in healthy adults. This study investigated the vinegar dosage (10 vs. 20 g), timing (during mealtime vs. 5 h before meal) and application (acetic acid as vinegar vs. neutralized salt) for reducing PPG. ***Methods:*** Four randomized crossover trials were conducted in adults (n = 9–10/trial) with type 2 diabetes (1 trial) or without diabetes (3 trials). All trials followed the same protocol: a standardized meal the evening prior to testing, an overnight fast (>10 h) and 2-hour glucose testing following consumption of a bagel and juice test meal (3 trials) or dextrose solution (1 trial). For each trial, PPG was compared between treatments using area-under-the-curve calculations 120 min after the meal. ***Results:*** Two teaspoons of vinegar (~10 g) effectively reduced PPG, and this effect was most pronounced when vinegar was ingested during mealtime as compared to 5 h before the meal. Vinegar did not alter PPG when ingested with monosaccharides, suggesting that the antiglycemic action of vinegar is related to the digestion of carbohydrates. Finally, sodium acetate did not alter PPG, indicating that acetate salts lack antiglycemic properties. ***Conclusions:*** The antiglycemic properties of vinegar are evident when small amounts of vinegar are ingested with meals composed of complex carbohydrates. In these situations, vinegar attenuated PPG by ~20% compared to placebo.

Introduction

In comparison to fasting blood glucose and hemoglobin A1c, postprandial glycemia (PPG) is considered the earliest dysglycemic marker for cardiovascular disease (CVD) [1]. Whereas fasting blood glucose is related to CVD only at concentrations indicative of impaired fasting glucose (≥ 5.6 mmol/l), PPG is linearly related to CVD risk across nondiabetic and diabetic ranges [2–4]. The adverse effects of elevated PPG, even when fasting blood glucose or hemoglobin A1c concentrations are within normal ranges, relate to the formation of free radicals and inflammatory mediators [5, 6].

Numerous oral hypoglycemic agents that specifically target PPG have been approved for the treatment of type 2 diabetes mellitus (T2D), including α-glucosidase inhibitors (e.g. acarbose and miglitol) and glinides (e.g. nateglinide and repaglinide). The therapeutic value of these drugs has been demonstrated to extend beyond managing T2D to reduce the risk for CVD in diabetic patients [7] and risk for T2D and CVD in individuals with im-

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paired glucose tolerance [8]. PPG is also lowered by the common food ingredient vinegar. A single vinegar dose (~20 g at 5% acidity) reduced PPG by up to 50% in healthy individuals [9–11], mirroring the demonstrated action of acarbose in patient populations [12]. Although the mechanism of action of vinegar is unclear, the acetic acid in vinegar may interfere with disaccharidase activity [13] and/or slow gastric emptying [14]. The purpose of this study was to investigate the dosage, timing and application of vinegar for reducing PPG.

Subjects and Methods

Participants

Four trials were conducted in separate subject populations. All participants (12/26 M/F; 21–79 years) were recruited from a campus population and surrounding communities via advertisements. Participants in three of the trials were healthy by self-report and had not been diagnosed with a chronic disease including diabetes or prediabetes. Individuals diagnosed with T2D, but otherwise healthy and not taking insulin, were specifically recruited for the fourth trial. These individuals took at least one hypoglycemic medication daily, and all prescription medication use in these individuals was stable over the course of the trial. Written informed consent specific to each trial was obtained from subjects, and all trials were approved by the Institutional Review Board at Arizona State University.

Study Protocol

The four trials were conducted using a double-blind, randomized, crossover research design. Each participant in each trial received all trial treatments with 1 week separating treatments: trial 1 had four treatment arms, trials 2 and 4 had three treatment arms, and trial 3 had two treatment arms. The same protocol was followed within each trial: a standardized meal the evening prior to testing, an overnight fast (>10 h), and 2-hour glucose tolerance testing following consumption of a bagel and juice test meal (trials 1, 2 and 4) or a dextrose solution (trial 3). Subjects were instructed not to participate in moderate-intense exercise the day prior to testing, and the same, standardized evening meal (a sub sandwich, chips and cola drink) was consumed each evening prior to testing followed by an overnight fast (10–12 h). Immediately prior to testing, a fasting blood sample was collected, and subjects were randomly assigned to consume the vinegar treatment or placebo followed by the test meal (white bagel, 20 g butter and 200 g juice) or dextrose solution. The foods were consumed under observation within a 10-min period, and this protocol was repeated weekly until all treatment arms were completed. For trial 1, the quantity of bagel ingested by individual participants was adjusted to provide ~1 g carbohydrate/kg body weight. In trials 2 and 4, a single 114-gram white bagel was consumed by participants and the bagel, butter and juice provided 75 g carbohydrates and 420 kcal. In trial 3, the bagel meal was replaced with 75 ml orange flavored dextrose solution (75 g glucose and 300 kcal, SUN-DEX; Fisher HealthCare, Houston, Tex., USA). All food was carefully measured and prepared fresh immediately prior to administration. Additional blood samples were collected at 30-min intervals after the meal for 2 h; subjects rested quietly during this postprandial period.

Vinegar Treatments

Commercially purchased apple cider vinegar (Heinz, Pittsburgh, Pa., USA) was used in trials 1, 3 and 4, and commercially purchased red raspberry vinegar (Star Fine Foods, Fresno, Calif., USA) was used in trial 2. All vinegars were 5% acetic acid as indicated by the manufacturer. Test drinks were carefully measured and prepared fresh. The vinegar aliquot was diluted with water to 40 g, sweetened with 1 teaspoon saccharine and colored with 1 drop food color. Subjects, as well as the investigator administering the drinks, were unaware of the contents of the test drink. The intense sweetness of the test drinks, in association with the bright red, blue or green color of the drink, fairly concealed the presence of vinegar. The placebo drinks were prepared in an identical manner but minus the vinegar. In blind taste tests, although subjects rated the vinegar containing drinks as slightly less palatable compared to placebo drinks, ratings between drinks did not differ significantly.

Trial 1. This trial examined whether small amounts of vinegar (2–20 g) possessed antiglycemic effects. Four test drinks were administered in this trial with 1 week separating each test session: 20 g vinegar (1 g acetic acid), 10 g vinegar (0.5 g acetic acid), 2 g vinegar (0.1 g acetic acid) and placebo (0 g acetic acid).

Trial 2. This trial examined whether the antiglycemic effect of vinegar persisted for 5 h after consumption. For this trial only, participants were instructed to consume a small breakfast at about 7 a.m. (1 oz dry cereal, 1 cl milk, 1 oz cheese and 1 small apple) and not to consume any other food or beverage except water until they arrived at the test site exactly 5 h later for PPG measurements with the bagel meal. Three treatments were administered with 1 week separating each test session: 20 g vinegar (1 g acetic acid) administered 2 min prior to the test meal, 20 g vinegar administered at breakfast 5 h prior to the test meal, and placebo administered 2 min prior to the test meal.

Trial 3. This trial examined whether the antiglycemic property of vinegar was dependent on the form of carbohydrate consumed. Two treatments were administered with 1 week separating test sessions: 20 g vinegar (1 g acetic acid) or placebo administered 2 min prior to the ingestion of dextrose.

Trial 4. This trial examined whether a 'vinegar pill' (e.g. the neutralized salt of acetic acid, sodium acetate) possessed antiglycemic effects in individuals with T2D. Three treatments were administered with 1 week separating each test session: 20 g vinegar (1 g acetic acid) administered 2 min prior to the test meal, 1.2 g sodium acetate (dissolved in 40 g water in place of the vinegar aliquot equating to 1 g acetate) administered 2 min prior to the test meal, and placebo administered 2 min prior to the test meal.

Blood Analysis

In trials 1 and 2, capillary blood 0, 30, 60, 90 and 120 min after the meal was analyzed for glucose using a calibrated glucometer (OneTouch *Ultra* glucometer; LifeScan, Milipitas, Calif., USA). Timing for the 60-min blood sampling was delayed 17 min for 2 participants in trial 1; hence, glycemia data are reported only for the 8 remaining participants. In trials 3 and 4, plasma glucose from venous blood was analyzed by standard enzymatic procedures (Sigma Diagnostics, St. Louis, Mo., USA). Plasma insulin

from fasting venous blood was determined by radioimmunoassay (ICN Pharmaceuticals, Costa Mesa, Calif., USA).

Statistical Analysis

Data are reported as means ± SE. An independent t test, or a one-way analysis of variance with the Tukey post hoc test, was utilized to determine differences between means at baseline. PPG was calculated as the incremental area-under-the-curve 120 min after the meal using the trapezoidal rule. Data were not normally distributed, and the nonparametric Friedman test was utilized to compare means. The effect size statistic, partial η_p^2, was used to indicate the proportion of variance of the dependent variable explained by the independent variable. Trial sample sizes ranged from 8 to 10 providing approximately 65% power to observe a 20% change in PPG. $p \leq 0.05$ indicated statistical significance, and the Statistical Package for the Social Sciences (SPSS 15.0 for Windows 2006; SPSS, Chicago, Ill., USA) was used for all analyses.

Results

Baseline characteristics of the four sample populations varied by age and/or by body mass index (table 1). Subjects in trial 4 with T2D had fasting plasma glucose and insulin concentrations significantly higher than the subjects in trials 1–3. Gender, age, body mass index and/or body weight, however, were not significantly correlated to PPG in any of the trials. Fasting glucose concentrations did not significantly differ between the treatment arms in trials 1–3; however, in trial 4, in the individuals with T2D, fasting glucose concentrations varied by 10% (range: 7.3–8.1 mmol/l; $p < 0.05$).

In trial 1, PPG was reduced by 23–28% by the 10-gram vinegar dosage (0.5 g acetic acid) as compared to the 2 g vinegar dosage (0.1 g acetic acid) or placebo treatment ($p = 0.050$; fig. 1a); however, the 20-gram vinegar dosage reduced PPG only marginally (6–12%). The incremental AUC values were 157 ± 28, 129 ± 21, 178 ± 21 and 167 ± 22 mmol·min/l for the 20-, 10-, 2- and 0-gram vinegar dosages, respectively. In trial 2, vinegar ingested with the test meal reduced PPG by 19% compared to placebo ($p = 0.169$; fig. 1b), but vinegar ingested 5 h prior to the test meal did not appear to impact on PPG relative to placebo (incremental AUC values: 266 ± 45, 331 ± 38 and 330 ± 38 mmol·min/l, respectively).

Following the ingestion of a dextrose drink (trial 3), mean PPG after the vinegar treatment was 90% greater than that after the placebo treatment ($p = 0.059$, fig. 1c). The incremental AUC values were 103 ± 38 and 54 ± 43 mmol·min/l for the vinegar and placebo treatments, respectively. In individuals with T2D (trial 4), PPG was reduced (13–17%) by the vinegar treatment compared to the sodium acetate and placebo treatments ($p = 0.097$; fig. 1d), and the incremental AUC values were 540 ± 24, 622 ± 38 and 653 ± 39 mmol·min/l for the vinegar, sodium acetate and placebo treatments, respectively. In three of the four trials, statistical significance was not achieved; however, effect sizes were >0.30 (a moderate difference), suggesting that the changes observed were physiologically relevant.

Table 1. Baseline characteristics of subjects in trials 1–4

Trial	Males/females	Age years	BMI	Fasting glucose, mmol/l	Fasting insulin, mU/l
1	4/6	35 ± 4^{a}	27.5 ± 1.2^{a}	5.3 ± 0.1^{a}	7.8 ± 1.7^{a}
2	2/7	50 ± 5^{b}	33.7 ± 2.3^{b}	5.4 ± 0.1^{a}	N/A
3	2/8	$38 \pm 4^{a, b}$	26.3 ± 1.0^{a}	5.2 ± 0.1^{a}	16.8 ± 1.8^{a}
4	4/5	69 ± 2^{c}	$31.4 \pm 1.4^{a, b}$	7.7 ± 0.6^{b}	30.4 ± 6.2^{b}

Means ± SE; means in the same column with different superscripts differ significantly, $p \leq 0.05$ (one-way ANOVA; Tukey post hoc test). BMI = Body mass index.

Discussion

The antiglycemic effect of single-dose vinegar has been documented [9–11]. The research presented herein demonstrated that vinegar ingestion at mealtime reduced PPG by about 20% on average compared to the placebo treatments. This reduction is comparable to those noted in trials that assessed the effects of α-glucosidase inhibitors in patients with impaired glucose tolerance [15] and T2D [16].

Trial 1 demonstrated that 10 g (~2 teaspoons) of 5% acidity vinegar reduced PPG after 2 h by 23% compared to placebo ($p = 0.05$). This amount of vinegar is about one half that demonstrated to reduce PPG previously [9, 11]. This smaller dose of vinegar equates to that in a serving of vinaigrette dressing, typically composed of 2 parts oil/1 part vinegar. Hence, a green salad with 2 tablespoons of vinaigrette dressing at mealtime would provide a medicinal dose of vinegar; or 2 teaspoons of vinegar could be consumed palatably in hot tea with lemon at mealtime.

In trial 1, however, the higher amount of vinegar (20 g vinegar containing 1 g acetic acid), a dosage used successfully to reduce PPG in previously published reports as well as in trials 2 and 4 of this report, reduced PPG by only 6–10%. The reason for this discrepancy is not clear.

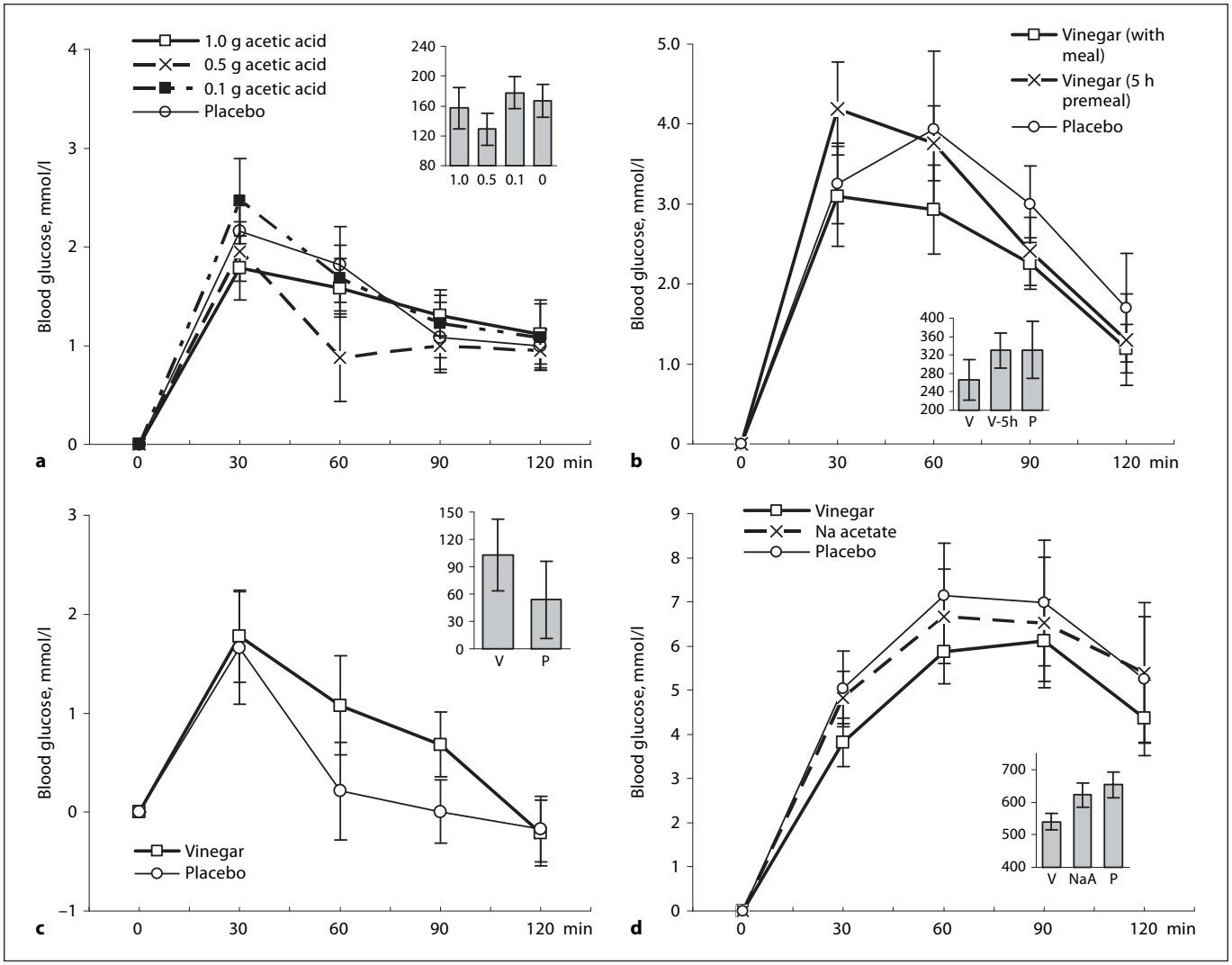

Fig. 1. Blood glucose responses (means ± SE) at 0, 30, 60, 90 and 120 min for trials 1–4. **a** Acetic acid (0, 0.1, 0.5 and 1.0 g as vinegar) consumed immediately prior to the test meal (bagel + juice) in 8 healthy adults. p = 0.050; η_p^2 = 0.544. **b** Acetic acid (1.0 g) consumed as vinegar immediately prior to or 5 h prior to the test meal versus placebo and test meal ingestion in 9 healthy adults. p = 0.169; η_p^2 = 0.348. **c** Acetic acid (1.0 g) consumed as vinegar versus placebo ingested immediately prior to a 75-gram dextrose load in 10 healthy adults. p = 0.059; η_p^2 = 0.394. **d** Acetate (1.0 g) consumed as vinegar or as sodium acetate diluted in water immediately prior to the test meal versus placebo and test meal ingestion in 9 healthy adults with type 2 diabetes. p = 0.097; η_p^2 = 0.328. The inserted charts represent mean incremental area-under-curve data (mmol × min/l). p value for area-under-curve calculation (Friedman test); η_p^2 represents effect size using partial η_p^2 statistic.

In fact, Ostman et al. [11] observed an inverse dose-response relationship between the level of acetic acid (1.0, 1.4 and 1.8 g) and the PPG response to a 50-gram complex carbohydrate load.

The timing of the vinegar dose was examined in trial 2, and although the data were not statistically significant, the effect size was large (η_p^2 = 0.348), indicating that vinegar ingestion at mealtime provided a moderate physiological benefit. The antiglycemic effect of vinegar may relate to delayed gastric emptying rates [14] or to the inhibition of digestive enzymes [13]. In cultured Caco-2 cells, the addition of acetic acid, but not other organic acids such as citric or lactic acids, inhibited sucrase, maltase, trehalase and lactase activity [13]. The α-glucosidase inhibitors, e.g. acarbose, reduce PPG by inhibiting digestive enzymes; the resultant delay in carbohydrate digestion slows gastric

emptying by magnifying the incretin feedback response [17]. Therefore, to be effective, these drugs are to be consumed with the first bites of each main meal. For similar reasons, this may be the situation for vinegar.

Trial 3 provided in vivo evidence that the antiglycemic property of vinegar is related to the inhibition of starch digestion. In this trial, the carbohydrate load was composed entirely of the monosaccharide dextrose, and the vinegar treatment did not reduce PPG at any time point. In fact, PPG was slightly elevated for the vinegar treatment compared to placebo ($p = 0.059$). These data suggest that the antiglycemic effect of vinegar is best realized when ingested with foods composed of complex carbohydrates and that vinegar may not attenuate PPG following the consumption of foods sweetened with corn syrups or dextrose, as is the case for many processed beverages and foods.

In animal models, acetate ingestion has been demonstrated to reduce PPG in some studies [18] but not in others [19]. Thus, it is plausible that the antiglycemic effects observed with vinegar (aka, acetic acid) ingestion may be at least partially achieved with acetate ingestion. Moreover, encapsulated acetate salts would simplify the medicinal use of acetate for controlling PPG. In trial 4, the mealtime antiglycemic effect of 1 g acetate administered orally as a sodium acetate solution or as vinegar was examined in individuals with T2D, and the results suggested that only acetic acid was effective at attenuating PPG. Hence, the neutralized salt of acetic acid does not appear to possess antiglycemic properties when administered medicinally.

Taking steps to reduce PPG is recommended by the American Diabetes Association to limit complications of diabetes [20], and the therapeutic value of hypoglycemic agents that target PPG in non-diabetic populations has been demonstrated in several clinical trials [8, 21]. Considering the accumulating evidence supporting an antiglycemic effect of vinegar, the medicinal use of vinegar at mealtime may be considered alongside other dietary manipulations currently recommended for reducing PPG: monitoring total grams of dietary carbohydrate and utilizing the glycemic index of individual food items when preparing meal plans. However, it should be noted that in patients with type 1 diabetes mellitus and diabetic gastroparesis, vinegar ingestion (30 ml) delayed the gastric emptying rate nearly 40%, which may increase the frequency of hypoglycemic events [22].

In summary, data from these four trials suggest that small amounts of vinegar (2 teaspoons) ingested with meals composed of complex carbohydrates attenuate PPG by about 20%. Sample sizes in these trials were small, and the reductions for meal-induced PPG by vinegar was statistically significant for one trial ($p = 0.05$) but not the other two trials ($p = 0.097$ and $p = 0.169$). Yet, any diet strategy that attenuates PPG is welcomed since the magnitude of these glucose excursions has been implicated in the progression of the diabetic state as well as atherosclerotic disease.

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