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## Short communications

# Vinegar ingestion at mealtime reduced fasting blood glucose concentrations in healthy adults at risk for type 2 diabetes

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## ABSTRACT

This 12-week pilot study examined effects of vinegar on markers of type 2 diabetes in at-risk adults. Participants ( $n = 14$ ) ingested 750 mg acetic acid as a vinegar drink or a control pill (40 mg acetic acid) twice daily at mealtime. Blood glucose (fasting and 2-h postprandial) was recorded daily. Fasting blood collected at weeks 0 and 12 was analyzed for insulin and glycated hemoglobin. Average change in fasting glucose was reduced in the vinegar group versus control group ( $-0.91 \pm 0.27$  versus  $-0.26 \pm 0.17$  mmol/l) ( $p = 0.05$ ). Average change in 2-h postprandial glucose, insulin and glycated hemoglobin did not vary between groups. Fasting breath hydrogen at week 12 was elevated 19% in the vinegar group versus control group suggesting an increase in colonic fermentation in the vinegar group. These data indicate that vinegar, a simple addition to meals, has antiglycaemic effects in adults at-risk for type 2 diabetes, possibly related to carbohydrate maldigestion.

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## 1. Introduction

The prevalence of type 2 diabetes in the US and worldwide approaches 10% and is predicted to rise in the coming decades. More disconcerting, the risk of developing type 2 diabetes is estimated to be as high as 50% for US adults >65 y (Danaei et al., 2011; Tabák, Herder, Rathmann, Brunner, & Kivimäki, 2012). The American Diabetes Association assesses risk for type 2 diabetes based on impaired fasting glucose (fasting concentrations >5.5 mmol/L) or impaired glucose tolerance (2 h post-load concentrations >7.7 mmol/L). Strategies to reduce risk and slow

progression to type 2 diabetes are urgently needed. Weight management using prudent diet approaches and physical activity are effective at delaying progression to type 2 diabetes in high-risk individuals (Tabák et al., 2012; Knowler et al., 2002). However, much of the research has focused on drug therapies to reduce disease incidence, particularly antidiabetic agents such as alpha-glucosidase inhibitors, thiazolidinediones and biguanides. These agents reduced progression to type 2 diabetes by 40–60% in high-risk adults (Tabák et al., 2012). However, the cost, access and toxicities associated with pharmaceutical medications limit their usefulness.

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Abbreviations: BMI, body mass index; A1c, glycated hemoglobin  
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Since antiquity, vinegar has been used medicinally; moreover, it is inexpensive, shelf-stable and a common ingredient in many cuisines. Numerous investigations have verified the antiglycaemic effects of vinegar at mealtime in both healthy adults and adults with type 2 diabetes (Johnston & Gaas, 2006). Although the mechanisms of vinegar action are unclear, acetic acid, the defining ingredient of all vinegars, may interfere with carbohydrate digestion, promote glucose uptake by muscle, and/or increase  $\beta$ -cell insulin secretion (Ogawa et al., 2000; Fushimi et al., 2001; Seok et al., 2012). In adults with type 2 diabetes, daily ingestion of vinegar lowered fasting glucose concentrations and glycated hemoglobin (A1c) (White & Johnston, 2007; Johnston, White, & Kent, 2009). To date there has not been a long-term trial examining the efficacy of daily vinegar ingestion for lowering markers of diabetes in at risk adults.

## 2. Methods

### 2.1. Participants

Healthy adults at risk for type 2 diabetes (diagnosed prediabetes or a fasting blood glucose measure  $>5.55$  mmol/l at study entry) were screened for diabetic medications, but other stable medication use ( $>3$  months) was permitted. Data are reported for individuals who completed the 12-week study (14 of 19 participants; 13 F and 1 M). All participants provided written informed consent, and the study was approved by the Arizona State University Institutional Review Board.

### 2.2. Study design

Participants were paired by gender, age, body mass index (BMI) and prediabetes diagnosis and randomly assigned to the vinegar (drink) or control (pill) group. Participants maintained customary diet and activity patterns during the study and measured blood glucose concentrations twice daily (upon waking in a fasted state and 2-h after the evening meal) using a calibrated glucometer with memory (ACCU-CHEK, Avia meter system, Indianapolis, IN). Glucometer data were downloaded by study investigators at study weeks 6 and 12. At study weeks 0 and 12, fasting venous blood samples were collected for insulin and A1c analyses, and at week 12, fasting breath hydrogen and methane samples were collected.

The study treatments (vinegar: 8 oz vinegar drink; control: 1 vinegar pill) were ingested twice daily with meals. The commercially available vinegar drink (Bragg Organic Apple Cider Vinegar Drink Sweet Stevia, Bragg Live Food Products, Santa Barbara, CA) contained 1 tablespoon vinegar (750 mg acetic acid) per 8 oz. The commercially available vinegar pills (Apple Cider Vinegar tablets, General Nutrition Corporation, Pittsburgh, PA) contained trace amounts of acetic acid (40 mg/tablet).

### 2.3. Blood and breath samples

Venous blood samples were immediately analyzed for A1c using the DCA Vantage Analyzer (Siemens Healthcare Diagnostics, Tarrytown, NY) and plasma was extracted for later

insulin analysis (Human Insulin-Specific RIA, Millipore Corporation, Billerica, MA). Three consecutive breath samples were attained in the fasting state using a mouthpiece and collection bag (QuinTron AlveoSampler bags model#QT00842-P, QuinTron Instrument Company, Milwaukee, WI). Samples were transferred to the BreathTracker SC from QuinTron and analyzed for hydrogen and methane. Values from the three breath samples were averaged after correction using carbon dioxide measurement. Breath hydrogen and breath hydrogen + methane  $\times 2$  values are reported.

### 2.4. Statistical analysis

Results are expressed as the mean  $\pm$  SE. The Mann Whitney U test was used to test differences between means at baseline. Univariate analyses were used to identify significant differences in the outcome variables controlling for potential covariates and Pearson's correlation was used to examine relationships between variables (Predictive Analytics Software Statistics package 19.0, IBM, 2009).  $P$  values  $\leq 0.05$  were considered significant. Seven participants completed the study in each group, and complete glucometer data were available through week 7 for these participants. In weeks 8–12, the last data point was carried forward for 3 individuals with missing glucometer data ( $n = 1$  for drink and  $n = 2$  for pill). Breath hydrogen and methane measures were log transformed prior to analyses. One participant in the vinegar group, a vegetarian, displayed elevated fasting breath hydrogen ( $>3$  SD from the mean) and was removed from the breath gases analyses.

## 3. Results

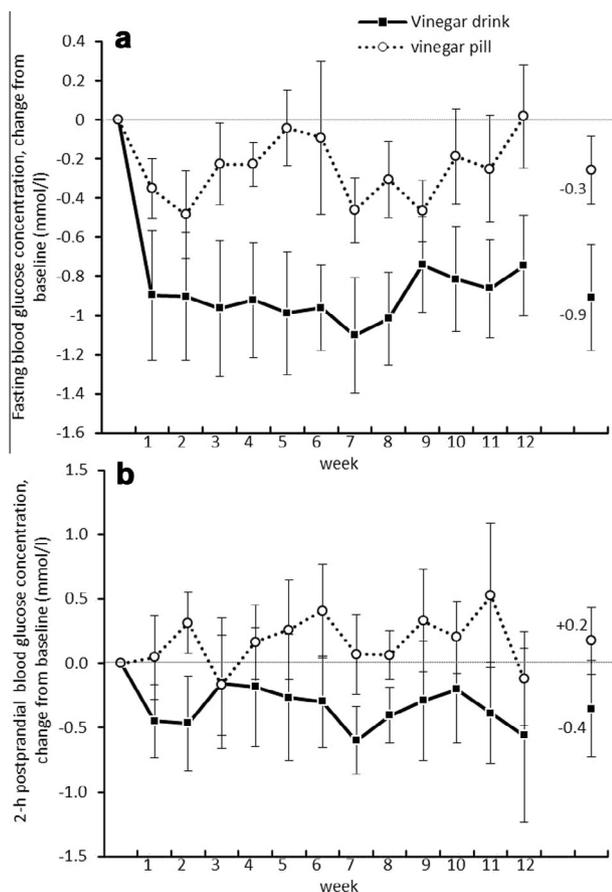
Baseline characteristics did not differ between groups (Table 1). Reported treatment compliance was 89 and 77% of study days for the drink and pill groups respectively. At baseline, fasting glucose concentrations were related to age ( $r = 0.651$ ,  $p = 0.01$ ) and A1c ( $r = 0.647$ ,  $p = 0.01$ ), and fasting glucose concentrations and A1c were elevated in the participants diagnosed with prediabetes compared to the other participants ( $6.93 \pm 0.43$  versus  $5.67 \pm 0.28$  mmol/l,  $p = 0.04$  and  $6.0 \pm 0.1$  versus  $5.2 \pm 0.1\%$ ,  $p = 0.003$ ).

Daily fasting glucose concentrations were averaged weekly for a total of 12 means. The pre-study, 6-day baseline measurement was subtracted from each weekly average to compute incremental data (Fig. 1a). Controlling for age and prediabetes diagnosis, the average change in fasting glucose differed significantly between groups ( $-0.91 \pm 0.27$  and  $-0.26 \pm 0.17$  mmol/l for the vinegar and control groups respectively;  $p = 0.05$ ). The average changes in fasting glucose were similar at study weeks 1–6 ( $-0.94 \pm 0.30$  and  $-0.24 \pm 0.19$  mmol/l;  $p = 0.08$ ) and 7–12 ( $-0.88 \pm 0.24$  and  $-0.28 \pm 0.17$  mmol/l;  $p = 0.03$ ). Fig. 1b depicts the incremental change in the weekly 2-h postprandial glucose by treatment. The average change in 2-h postprandial glucose did not differ significantly by group ( $-0.35 \pm 0.37$  and  $0.18 \pm 0.26$  mmol/l for the drink and pill groups respectively;  $p = 0.21$ ). Body weight, insulin concentration and A1c percentages did not vary significantly over time or between groups during the 12-week study.

**Table 1 – Participant characteristics at baseline by treatment group.**

	Vinegar (n = 7)	Control (n = 7)	P
Gender (F/M)	7/0	6/1	
Prediabetes diagnosis	3	5	
Age (y)	48.1 ± 5.2	43.9 ± 6.2	0.90
Weight (kg)	75.5 ± 6.2	76.2 ± 7.5	1.00
BMI (kg/m <sup>2</sup> )	29.2 ± 2.2	27.7 ± 2.0	0.71
Fasting glucose (mmol/L)	6.7 ± 0.5	6.0 ± 0.3	0.38
2 h postprandial glucose (mmol/L)	7.3 ± 0.7	6.5 ± 0.4	0.46
Insulin (mIU/mL)	17.3 ± 3.0	20.7 ± 5.2	0.81
HbA1c (%)	5.6 ± 0.2	5.7 ± 0.2	0.62

Note: P represents Mann Whitney U test



**Fig. 1 – Weekly change in blood glucose concentrations (a) after an overnight fast and (b) 2-h after the evening meal for the two trial conditions: vinegar drink (n = 7) or vinegar pill (control condition, n = 7). Values shown are the mean ± SE of duplicate determinations. Complete data were available through week 7; the last data is carried forward for three data points in weeks 8–12 (n = 1 for drink and n = 2 for pill). Labeled points at right represent the 12-week average change by condition (p = 0.05 and 0.21 for the fasting and postprandial glucose concentrations respectively; univariate analysis).**

Fasting breath hydrogen was significantly correlated with age ( $r = -0.628$ ,  $p = 0.02$ ) and the hydrogen + methane × 2 values correlated weakly with BMI ( $r = -0.486$ ,  $p = 0.09$ ).

Controlling for these covariates, fasting breath hydrogen differed significantly between groups at week 12 ( $4.3 \pm 1.1$  and  $3.6 \pm 1.4$  ppm for the vinegar and pill groups respectively;  $p = 0.05$ ). The hydrogen + methane × 2 values also differed significantly between groups at week 12 ( $38.8 \pm 19.0$  and  $12.8 \pm 8.8$  ppm for the vinegar and pill groups respectively;  $p = 0.04$ ).

#### 4. Discussion

Weight management using prudent diet approaches and physical activity are effective at delaying progression to type 2 diabetes in at-risk individuals (Knowler et al., 2002; Saaristo et al. 2010). Yet, adherence to healthy lifestyle plans is poor, and much research has focused on diabetic medications to reduce the incidence of type 2 diabetes (DeFronzo & Abdul-Ghani, 2011). The alpha-glucosidase inhibitor acarbose, which improves glucose tolerance by slowing carbohydrate digestion, reduced progression to type 2 diabetes in at risk individuals by 25% (Chiasson et al., 2002). Metformin, a widely prescribed biguanide that is effective for lowering glucose production in the liver and improving insulin sensitivity in muscle, was shown to reduce progression to type 2 diabetes by about 30% in at risk populations (Knowler et al., 2002; Ramachandran et al., 2006). Thiazolidinediones, which increase hepatic and peripheral insulin sensitivity by promoting peroxisome proliferator-activated receptor gamma activity, reduced the incidence of type 2 diabetes in high-risk individuals by 60% (DREAM Trial Investigators et al. 2006). In these trials, since the drugs reduced fasting glucose concentrations, the incidence of diabetes diagnoses over time was reduced; however, toxicities were noted, including gastrointestinal side effects for acarbose and a significant increased risk of congestive heart failure for the thiazolidinedione rosiglitazone.

This study in healthy individuals at risk for type 2 diabetes demonstrated that a simple diet strategy, regular vinegar ingestion (1 tablespoon at mealtime twice daily), resulted in greater reductions in fasting blood glucose concentrations than daily metformin or rosiglitazone use ( $-0.89$  versus  $-0.22$  and  $-0.50$  mmol/l respectively) (Knowler et al., 2002; DREAM Trial Investigators et al. 2006). This effect of vinegar is particularly noteworthy when the cost, access and toxicities associated pharmaceutical medications are considered.

Although 2-h postprandial glucose concentrations were consistently below baseline levels for the vinegar group, and these values for the control group were generally elevated above baseline levels, postprandial glucose concentrations did not differ between groups during the study. In hindsight, the 30-min postprandial glucose concentration might have been a better indicator of glucose control in this non-diabetic population. Also, controlled feeding trials have demonstrated that the antiglycaemic effect of acetic acid is restricted to meals composed of complex carbohydrates with high glycaemic responses (van Dijk, Tummars, Hamer, & van Loon, 2012; Liatis et al., 2010). Meal composition was not controlled in the present study; hence, vinegar-related reductions in postprandial glucose concentrations would vary based on the type and amount of carbohydrate present in the meal.

The timing of vinegar ingestion (immediately prior to the mid-day and evening meals) was based on a proposed mechanism of action: the acetic acid-induced suppression of carbohydrate digestion. In cultured Caco-2 cells, acetic acid treatment significantly decreased activity of the disaccharidases sucrase, maltase, trehalase and lactase whereas treatment with other organic acids (citric, succinic, L-malic, L-lactic, L-tartaric and itaconic acids) did not affect disaccharide activity (Ogawa et al., 2000). These data are supported by clinical investigations showing no effect of vinegar on postprandial glycemia when administered with an oral glucose (e.g., monosaccharide) load (Johnston, Steplewska, Long, Harris & Ryals, 2010; van Dijk et al., 2012). Carbohydrate maldigestion can be detected by measuring breath hydrogen, a marker of gut hydrogen and colonic fermentation. Breath hydrogen testing typically encompasses repeated measurements for up to 6 h following a carbohydrate challenge; however, fasting breath hydrogen can detect prolonged excretion of hydrogen in certain populations (Casellas & Malagelada, 2003). At week 12 of the study, fasting breath hydrogen was significantly elevated (+19%) in the vinegar group as compared to the control group. Furthermore, the hydrogen + methane  $\times 2$  value was raised over 3-fold in the vinegar group as compared to the control group. Methane is also a product of colonic fermentation in individuals who are methane producers (30–50% of adults). Measuring hydrogen alone will underrepresent colonic fermentation since methane production consumes hydrogen (specifically, methane consumes twice the hydrogen as conveyed by the formula: hydrogen + methane  $\times 2$ ) (Knudsen & DiPalma, 2012; Narvaez & DiPalma, 1988). Although these data are very preliminary and must be interpreted cautiously as baseline data were not collected, breath hydrogen testing may be a useful tool for investigating the mechanism of action for vinegar.

Although A1c was not reduced significantly by daily mealtime vinegar ingestion, mean values were reduced 0.14%, a reduction greater than that noted in the metformin trial (~0.05%) (Knowler et al., 2002) but similar to that achieved in an earlier vinegar trial conducted in individuals with diagnosed type 2 diabetes (–0.16%) (Johnston et al., 2009). The lack of a significant reduction in A1c may be explained by the fact that baseline A1c values for the study population (5.7  $\pm$  0.1%; range 4.8–6.5%) were below target values established for patient populations (6.5–7%) (Teoh, Home & Leiter, 2011).

Interestingly, hemoglobin A1c and fasting glucose concentrations were slightly reduced in the control group instructed to ingest commercial vinegar pills at mealtime (–0.07% and –0.26 mmol/l versus baseline). The pills contained a trace amount of acetic acid, 5% of that in the vinegar drinks. Previous research suggested that 1–2 tablespoons of vinegar at mealtime is the effective dosage (equating to 750–1500 mg acetic acid) (Ostman, Granfeldt, Persson & Björck, 2005); however, future research should examine whether small amounts of vinegar have beneficial effects on blood glucose concentrations in high risk populations. Acetic acid is the defining component of all vinegars (Compliance Policy guides Sec. 562.100, US Food and Drug Administration), and commercially sold vinegars must contain at least 4% acetic acid (4 g acetic acid per 100 ml).

Strategies to treat prediabetes and slow progression to type 2 diabetes are urgently needed. This research provides evidence that a simple diet change, the addition of vinegar to meals each day, reduced fasting glucose significantly in individuals at risk of developing type 2 diabetes. This effect was immediate (occurring within the first week of treatment) and sustained during the study period; moreover, this effect was noted without any further changes to eating patterns. Elevations in colonic fermentation as evidenced by breath hydrogen and methane measurements suggest that the antiglycaemic effect of vinegar is related in part to carbohydrate maldigestion. This research adds to the growing literature demonstrating the antiglycaemic properties of vinegar. Purposeful integration of vinegar or acetic acid into the food matrix, beyond the standard dressings and sauces, may facilitate reductions in blood glucose concentrations in both those diagnosed with type 2 diabetes and those at risk for this disease.

### Author contributions

All authors contributed to study design, implementation, data analyses and manuscript review. C.J. wrote the manuscript.

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