

Integrative Medicine

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the latest developments in integrative therapies [ALERT]

HOMEOPATHY

ABSTRACT & COMMENTARY

Homeopathy for Cold Symptoms in Young Children

By David Kiefer, MD, Editor

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Dr. Kiefer reports no financial relationships relevant to this field of study.

SYNOPSIS: A cough syrup containing homeopathic remedies improved cold symptoms more than placebo during the first day of treatment only.

SOURCE: Jacobs J, Taylor JA. A randomized controlled trial of a homeopathic syrup in the treatment of cold symptoms in young children. *Comp Ther Med* 2016;29:229-234.

What to do when young children have an upper respiratory infection, and symptomatic relief seems hard to come by? This can be a difficult task for parents and healthcare providers alike. Into this quandary stepped two researchers from Seattle, whose aim was to test the efficacy of homeopathy.

In this study, participants were recruited from a pediatric outpatient clinic. These recruits included children 2-5 years of age with a diagnosis of an upper respiratory tract infection and symptoms less than seven days; they were randomized to receive a homeopathic

cough syrup or placebo. Children were excluded if they had already taken a homeopathic remedy in the previous 48 hours, if they had asthma, or if they were prescribed medicines at that clinic visit or were taking medicine prescribed at a previous visit.

If the parents of the children elected to participate in the trial, they were asked to rate four of the child's symptoms (runny nose, cough, sneezing, and congestion) each on a scale of 0 (none) to 4 (severe). The treatment group received Hyland's Cold 'n Cough 4 Kids containing the seven remedies listed in Table 1. As an aside, the product used in this clinical trial

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Summary Points

- These investigators randomized 261 children 2-5 years of age to receive a cough syrup containing homeopathic remedies or placebo to be used as needed for three days.
- Compared to a baseline assessment, cold symptoms, such as cough, runny nose, and sneezing, improved in the homeopathy group more than placebo, but only in day 1 of treatment.
- By the end of the third day of treatment, there was no difference between the homeopathy and placebo groups.

included 6X and 12X homeopathic remedies. A 6X homeopathic remedy contains a substance that was diluted in a ratio of 1:10 six consecutive times, and a 12X remedy was diluted in that way 12 times. The syrup was sweetened with a glycyrrhiza extract, as was the placebo syrup, rendering both indistinguishable. The syrups were dosed one teaspoon (5 mL) every 4-6 hours as needed to treat cold symptoms up to a maximum of six times daily for three days.

Information about the changes in symptoms were recorded by the parents. Table 2 shows the rating systems used and includes overall symptoms, symptom changes, and side effects for the three-day treatment period. A follow-up phone call was made 5-10 days after enrollment to re-assess some of the variables. (See Table 2.) In addition, parents were asked about the child missing school or daycare, or if the parent missed work, as well as if the child was administered any other treatments during the study period. From the data resulting from the first line of Table 2, overall severity, a composite cold score (CCS), was created by adding the four scores for a total ranging from 0-16.

From the enrollment period, 261 children were eligible for randomization to the homeopathic syrup (n = 128) or the placebo syrup (n = 133). Out of this group of 261, 154 returned information after the syrup dosages and 162 returned the other information about symptoms, overall health, and function. There was no statistical difference between the groups who returned information or who didn't return information with respect to demographics and clinical characteristics. All told, 244 children "completed follow-up," although the researchers didn't specify what this meant.

Table 1: Homeopathic Remedies Contained in the Cough Syrup Used in this Study

- Allium Cepa (6X)
- Hepar Sulph Calc (12X)
- Natrum Muriaticum (6X)
- Phosphorus (12X)
- Pulsatilla (6X)
- Sulphur (12X)
- Hydrastis (6X)

The placebo and homeopathic groups did not differ significantly for any of the symptoms one hour after syrup dosage. However, for the twice-daily assessment of cold symptoms, some differences appeared. Compared to baseline, the homeopathic syrup group improved more than the placebo group for runny nose, cough, and sneezing (improvements ranged from -0.22 to -0.39; $P = 0.05-0.001$), but not congestion. Interestingly, this improvement occurred only for the first day, disappearing by day 3; that is, by the end of the treatment period, both groups had improved similarly. The CCS behaved similarly: For the first day, the homeopathic group had changed more from baseline than the placebo group. (See Table 3.) The CCS scores were not statistically significantly different for the other days.

Interestingly, 13 children in the homeopathy group were given ibuprofen the first morning after randomization, compared to only two in the placebo group ($P = 0.04$). Also, chest rubs were administered to 13 children in the homeopathy group but to only two in the placebo group the first morning ($P = 0.002$) and the second morning ($P = 0.028$). All functional outcomes were similar between the two groups for any day. When follow-up con-

Table 2: Parental Recording of Variables During the Three Days of Treatment with Cough Syrup

Variable	Time Variable Was Assessed	Measurement
Overall severity of runny nose, cough, sneezing, and congestion during the previous 12 hours	Morning and evening for three days; and 5-10 days after enrollment	4-point scale as with intake
Current runny nose, cough, sneezing, and congestion	One hour after each dose of syrup for a maximum of 10 entries	7-point Likert scale (“much worse” to “much improved”)
Changes in irritability, lethargy, fussiness, and appetite	One hour after each dose of syrup for a maximum of 10 entries	7-point Likert scale (“much worse” to “much improved”)
Side effects of the syrup	One hour after each dose of syrup for a maximum of 10 entries; and 5-10 days after enrollment	Free list
Five-item functional health scale	Once daily; and 5-10 days after enrollment	Referenced but not specified
Overall health	Once daily; and 5-10 days after enrollment	1 (totally well) to 10 (very sick)

Table 3: Changes in the Composite Cold Score from Baseline, a Negative Score Means More Improvement

	Day 1		Day 2		Day 3	
	Morning	Evening	Morning	Evening	Morning	Evening
Placebo	0.32*	-0.13**	-1.19	-1.25	-2.26	-2.27
Homeopathy	-0.13*	-1.25**	-1.82	-2.04	-2.46	-2.65

* $P = 0.005$ comparing the two; ** $P = 0.007$ comparing the two

tact occurred at day 5-10, cough severity was worse for the homeopathy group compared to placebo ($P = 0.009$). More side effects (9/75) were noted in the homeopathy group compared to the placebo group (2/79) ($P = 0.02$). None of the side effects were serious, but rather involved mostly gastrointestinal symptoms.

■ COMMENTARY

There is a gap in treatments available for young children with cold symptoms who are not prescribed a medicine. What are parents supposed to do? Many over-the-counter medicines are not appropriate for this age group, and symptomatic measures might only partially alleviate coughing and congestion that compromise sleep, eating, and the ability to return to schools or daycares and, therefore, return to work for parents.

Does this study highlight an intervention that could fill this niche? Possibly, but the clinical ramifications of these findings are narrow. After three days of the use of a cough syrup with seven homeopathic remedies, there was a slight improvement in some cold symptoms for the first day, but not thereafter. For suffering children (and parents), that is at least something, but it wasn't sustained for the rest of the trial, not to mention the fact that at day 5-10, the children's coughs were actually worse in that group. The researchers posited that it might be because of a rebound in symptoms after

stopping the therapy, but it could be considered actually a side effect — something worth factoring into our decision-making as clinicians until this study is replicated.

There are flaws in this trial that are worth keeping in mind. A large percentage of the study participants did not return the logs of symptoms after dosing nor the diaries with the other information about function and overall response to treatment. The authors mentioned this as a potential bias, even though the “returner” group and the “non-returner” group had statistically similar demographics and characteristics. Furthermore, no mention was made of the higher adverse effect rate in the homeopathy group. The conventional wisdom is that homeopathy either helps or doesn't have any effect; it is thought to be quite safe. Of course, skeptics of this type of therapy would say that it's safe because there is nothing actually in a homeopathic remedy. Regardless of the somewhat difficult-to-grasp mechanism of action, it's worth noting the adverse effects as we counsel our patients. Perhaps these remedies aren't as innocuous as previously thought.

There are not many clinical trials examining homeopathic remedies. From the landmark trial showing benefit in childhood diarrhea in Nicaragua¹ to trials on arnica homeopathics perioperatively,² this trial was a valiant effort. The authors mentioned other clinical trials using homeopathic remedies in upper respiratory

ry tract infections to which this current study contributes some information. For those children suffering from colds, benefiting minimally from conservative treatment, perhaps a day of relief, even a little bit, might be just what the doctor ordered. ■

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CARDIOVASCULAR DISEASE

ABSTRACT & COMMENTARY

Coffee or Tea? Implications for Cardiovascular Health

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Dr. Feldman reports no financial relationships relevant to this field of study.

SYNOPSIS: A large, multi-ethnic study found that tea consumption was associated with slowed progression of coronary artery disease and lowered risk of cardiovascular events when compared to never drinkers; coffee intake appears to have no measurable effect.

SOURCE: Miller PE, Zhao D, Frazier-Wood AC, et al. Associations of coffee, tea, and caffeine intake with coronary artery calcification and cardiovascular events. *Am J Med* 2017;130:188-197.

Tea or coffee? Both are among the most widely consumed beverages across the world.¹ Often, the choice is simple and based on preference and habit, but increasingly patients are asking which of these beverages is better for them and for health. Popular beliefs seem to sway toward tea as the more beneficial drink; however, definitive studies in this area still are pending.

We know that coffee consumption is related to a lower incidence of diabetes and improved endothelial function.² In June 2016, the World Health Organization declassified coffee as a carcinogen and noted it has protective effects against specific carcinomas (liver and uterus).³ However, studies of the effect of coffee on cardiovascular health have been less definitive and limited by homogeneity among the study group and perhaps confounded by the association of tobacco use with coffee consumption.

For centuries, tea — a beverage brewed from the leaves of the *Camellia sinensis* plant — was known throughout the Eastern Hemisphere for its widespread medicinal uses. As interest in possible health benefits of this plant spread to the western world in the 1980s, research into the properties and mechanism of action accelerated.⁴ Most researchers believe the benefits of tea derive from the abundant flavonoids in all forms of tea, although some forms have more antioxidants than others. Flavonoids, known to have antioxidant and anti-inflammatory properties, are found in most fruits and vegetables. Current studies suggest potential health benefits in many disorders, including specific carcinomas, hypertension,

Summary Points

- These researchers investigated an association between coffee or tea consumption and coronary artery disease, progression, and events.
- Tea drinkers: Study participants who reported drinking ≥ 1 cup of tea each day had a statistically significant slower rate of coronary artery calcium progression and a lower rate of cardiac events, including myocardial infarction, cardiac arrest, and stroke.
- Coffee drinkers: Study participants who reported drinking < 1 cup of coffee each day had an increased rate of cardiovascular events; there was no association found between any level of coffee drinking and progression of coronary artery calcium.
- Caffeine intake was analyzed independently and appeared to have no association with cardiovascular events.

and disorders of the eye, such as glaucoma and retinopathy, but studies have had conflicting results, particularly when field-tested on humans.^{4,5}

Noting that confounding variables, such as ethnic background, socioeconomic status, and nutritional

intake, contaminate many studies looking at tea, coffee, and cardiovascular disease, Miller et al studied a diverse population and controlled for these factors. The Multi-Ethnic Study of Atherosclerosis (MESA) is a prospective, multicenter study looking at the prevalence, risk factors, and progression of subclinical cardiac disease.⁶ The entire population-based group of 6,814 men and women (ages 44-84 years) enrolled in MESA were screened for eligibility in this study. Included for analysis in the Miller et al study were all MESA participants without baseline cardiovascular disease who completed the portion of the questionnaire regarding coffee and tea intake; 6,508 participants met these criteria for eligibility. More than 90% completed the interviews, beginning with a detailed questionnaire in 2000-2002, and continuing with yearly telephone calls and hospital record review until 2013.

Coffee and tea consumption were self-reported on the initial food-frequency questionnaire. Gradations of frequency ranged from never consumed to more than six cups daily. There was no distinction between caffeinated or decaffeinated coffee or tea, nor any distinction regarding black or green tea. No questions were asked regarding herbal or other commonly labeled “tea” products. Caffeine consumption was calculated separately from all available sources (food and beverage.)

Coronary artery calcium (CAC), a measure of subclinical atherosclerosis, was scored at baseline and progression or score changes were noted at follow-ups.

To eliminate confounding factors and isolate an association between tea or coffee and cardiovascular disease, the authors used four different models for analysis. Each model was progressively more comprehensive, ranging from Model 1, adjusting for age, sex, and ethnicity, to Model 4, adjusting for multiple factors, including lifestyle factors, medications, family history, and C-reactive protein and fibrinogen. A baseline ethnicity analysis showed higher tea intake among the Chinese American participants in the study. Given the lower incidence of cardiovascular events among this group, a sensitivity analysis was performed excluding this subgroup. This did not significantly affect the final results or study conclusions. See Table 1 for selected results from the study.

■ COMMENTARY

Does this comprehensive, meticulously designed, multi-ethnic, and multisite study with participants selected to represent a population-based sample definitively answer the question of which beverage (tea or coffee) conveys greater benefits for cardiovascular health? Not definitively, but the results of this study suggest that regular tea consumption is associated with decreased prevalence of CAC, slowed progression of CAC, and a decreased

incidence of cardiovascular events. However, there is no indication from this study that consumption of coffee or of caffeine (found in both beverages) is harmful or a factor in progression of CAC, and there is no association between caffeine use and incidence of cardiac events.

One question arising from the results of this study may be related to the coffee findings; that is, does a low consumption of coffee lead to an increased risk of a cardiovascular event? It is important to note that there was no association with increased accumulation of CAC among those reporting any frequency of coffee use, but an increase in actual cardiovascular events was noted among low frequency users. One explanation for this finding may be that some participants with known higher risk of cardiac problems chose to avoid coffee or were advised to do so. However, without more data the causality is unclear, and this remains an area for further investigation and research

The strengths of this study are considerable and include consistent results across a diverse population and multi-step efforts to eliminate confounding variables. The results of this study did not seem to differ among various ethnic groups and, in fact, remained valid even with exclusion of data from Chinese Americans (a group with a high consumption of tea and lower cardiovascular disease risk.) Likewise, the longitudinal nature of the study and the investigation of multiple related cardiovascular factors — including the prevalence of CAC, the progression of CAC, and the occurrence of cardiovascular events — are unique aspects that enhance the study value.

However, the prospective nature of this investigation does not allow room for changes in habit or of beverage consumption over time; the recording of beverage consumption was dependent solely on recall at the time of the baseline questionnaire. Thus, these results are best interpreted with the understanding that there is no information available regarding ongoing consumption of tea or coffee over the study period. Future studies designed to eliminate the need for recall and looking at ongoing use of these beverages will be helpful in contributing more to this field.

The observational nature of this study makes it difficult to move from association to causation. Future efforts should move toward more active, interventional studies. In doing so, understanding the effect from a specific type of tea (black, green, oolong — all with differing antioxidant content) also will help advance the field and allow better clinical recommendations. Designing a study to try to isolate the effect of tea (as opposed to the overall effect of a healthy lifestyle inclusive of tea) will help clarify this question of causation as well.

Table 1: Selected Results for Coffee vs. Tea Drinkers

Results were considered significant if *P* values (2-sided) were < 0.05. In this chart, significant results are bolded. All results are for Model 4, which includes the most comprehensive adjustment for confounding factors.

Results for Coffee Drinkers

	Never drink	< 1 cup daily	> 1 cup daily
CAC prevalence 1-99 at baseline (95% confidence interval)	1	1.07 (0.88-1.30)	1.02 (0.85-1.21)
CAC prevalence ≥ 100 at baseline (95% confidence interval)	1	1.18 (0.93-1.49)	1.10 (0.89-1.15)
CAC progression ratio (95% confidence interval)	1	1.11 (0.95-1.29)	1.06 (0.92-1.22)
Hazard ratio (95% confidence interval) between coffee and cardiovascular event	1	1.28 (1.02-1.61)	0.97 (0.78-1.20)

Results for Tea Drinkers

	Never drink	< 1 cup daily	> 1 cup daily
CAC prevalence 1-99 at baseline (95% confidence interval)	1	0.96 (0.81-1.12)	0.90 (0.73-1.12)
CAC prevalence ≥ 100 at baseline (95% confidence interval)	1	1.03 (0.86-1.24)	0.64 (0.49-0.84)
CAC progression ratio (95% confidence interval)	1	0.96 (0.85-1.09)	0.73 (0.61-0.87)
Hazard ratio (95% confidence interval) between coffee and cardiovascular event	1	0.92 (0.76-1.10)	0.71 (0.83-0.95)

Results for Caffeine Consumption

	Lowest tertile (< 55 mg/d)	Second tertile (55 to < 167 mg/d)	Third tertile (167-1,354 mg/d)
CAC prevalence 1-99 at baseline (95% confidence interval)	1	0.99 (0.84-1.18)	0.89 (0.74-1.07)
CAC prevalence ≥ 100 at baseline (95% confidence interval)	1	0.81 (0.66-1.00)	0.82 (0.66-1.01)
CAC progression ratio (95% confidence interval)	1	0.87 (0.76-1.00)	0.88 (0.76-1.02)
Hazard ratio (95% confidence interval) between coffee and cardiovascular event	1	0.96 (0.79-1.17)	0.87 (0.70-1.07)

Finally, it is useful to consider that “tea” in a strict sense is a beverage derived from the leaf of the *Camellia sinensis* plant. The various types of tea all come from the leaves of this plant but differ in the process of drying and fermentation.⁷ However, in many U.S. stores today, there are preparations promoted and advertised as “tea” that technically do not belong to this category. It may be that the original MESA questionnaire attempted to eliminate these “non-teas” by asking for green or black tea consumption, but the possibility of confusion due to widespread use of the term “tea” may have influenced consumption reporting.

Sometimes, it seems as if the world is divided between two types of people: tea drinkers and coffee drinkers. A

more nuanced view is that a definitive choice is neither necessary nor medically recommended; a healthy diet can include both beverages and, if desired, a person can tailor use to preference and specific health issues. Although a simple concept, this approach can be broadened — searching for inclusion rather than exclusion and enjoying diversity in diet are two important principles to consider when talking with patients about the important role of nutrition in health.

Clinically, the results of this study affirm that providers, backed by evidence that regular tea use is associated with a reduction in CAC and cardiac events, stand on firm ground recommending tea as an important component of a diet focused on cardiac health. Acknowledging

that coffee consumption appears safe from a cardiac viewpoint, but not necessarily protective, is an equally valid message. It is worth noting that this study did not attempt a head-to-head (or cup-to cup) comparison and that both beverages can contribute meaningfully to a multi-flavored, healthy lifestyle. ■

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VINEGAR

SPECIAL FEATURE

Health Benefits of Apple Cider Vinegar and Other Common Vinegars: A Review

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Dr. Fahey reports no financial relationships relevant to this field of study.

SYNOPSIS: A review of the literature to summarize the health benefits of apple cider vinegar and other common vinegars.

Vinegar has been used in households for more than 10,000 years, as seasoned vinegars for 5,000 years, and is sold in markets across the globe.¹ There are two types of vinegars made today: cider vinegar and normal vinegar. Vinegar can be made from many foods. Cider vinegar is made from fruit juices,² grapes, dates, figs, sugarcane, and apples, while normal vinegar can be made from grains, molasses, coconut, honey, beer, maple syrup, beets, and whey.³ Vinegars also are used in food production, from ketchups and mustard to sauces and mayonnaise. Vinegars contain bioactive compounds, the extra-nutritional constituents found in fruits and vegetables. These bioactive compounds are of many types, such as carotenoids, phytosterols, phenolic compounds, and vitamins C and E.^{4,5} More specifically, apple cider vinegar also contains organic acids (acetic acid, citric acid, formic acid, lactic acid, malic acid, and succinic acids) and phenolic compounds (gallic acid, catechin, epicatechin, chlorogenic acid, caffeic acid, and p-coumaric acid). All of these compounds instill vinegar with health benefits even when ingested in small amounts, such as acetic acid from vinegar as 0.3% of total food intake or 15-30 mL (1-2 tablespoons) of cider vinegar.⁶ These health benefits include reducing cholesterol and lipid levels, antioxidant properties, enzyme inhibitors, inhibitors of gene expression, antidiabetic effects,⁷ reduced blood pressure, prevention of heart disease, and antimicrobial properties.⁶

Summary Points

- Advise patients to be cautious about their vinegar consumption.
- Use organic, unfiltered, unprocessed apple cider vinegar, which is cloudy, meaning it contains the "mother."
- Oral: For diabetes, dilute 2 tablespoons apple cider vinegar in 8 ounces of water daily. For weight loss, drink diluted dose with high carbohydrate meals.
- Topical: Use with caution as chemical burns are common.

Vinegar is made using two biotechnological processes. First, the sugar contained in the food undergoes alcoholic fermentation in the presence of yeast, *Saccharomyces cerevisiae*, which converts the foodstuff to alcohol.⁶ Then, the alcohol is converted into acetic acid by acetous fermentation in the presence of acetic acid bacteria (*Acetobacter pasteurianus* and *Acetobacter polyoxogenes*). The Orleans method (conventional method) and the rapid methods (submerged and generator) are used for producing vinegars.⁸ The speed of vinegar production is affected by fermentation tem-

Table 1: Apple Cider Vinegar Benefits Reported Online

• Healthy blood sugar	• Morning sickness
• Weight loss	• Hiccups
• Lower cholesterol	• Inflammation
• Reduce hypertension	• Allergies and asthma
• Anticancer benefits	• Sinus infections
• Arthritis	• Anti-aging
• Detox support	• Urinary tract infections
• Gallbladder health	• Dementia
• Infections	• Acne
• Gut microbiome	• Sunburn
• Improved digestion	• Varicose veins
• Bloating and indigestion	• Insomnia
• Flatulence	• Dizziness
• Reflux	• Ear discharge
• Constipation	• Hair loss (topical)
• Diarrhea	• Headache
• Ulcers	• Mental alertness
• Candida infections	• Sore throat

perature, pH, yeast strains, sugar, and oxygen concentration.⁷

BIOACTIVE COMPOUNDS

Apple cider vinegar has a wide variety of health benefits listed online. Table 1 includes the variety of uses for apple cider vinegar on various health problems. The bioactive compounds and acetic acid in apple cider vinegar and other vinegar varieties contribute to the health benefits of vinegar.⁴ Bioactive compounds are “extra-nutritional constituents that typically are naturally occurring in small quantities in plant products and lipid-rich foods.”⁹ Epidemiological research has increased in the area of bioactive compounds because of their beneficial effect on chronic disease treatment and prevention.⁹ A diet rich in bioactive compounds, including flavonoids, anthocyanin, and others,¹⁰ has been shown to have significant health benefits.

Polyphenols prevent lipid peroxidation, hypertension, antiplatelet effects, and anti-inflammatory effects by improving endothelial function, hyperlipidemia, inflammation, DNA damage, and cancer.¹¹ Recent research on antioxidants has shown that they can prevent chronic disease. The most abundant antioxidants in vinegar are polyphenols and vitamins, both with a long history of fighting oxidation.⁶ The polyphenol pathway is directly correlated with the quality of cider vinegars because polyphenols contribute to the acidity, sharpness, hue, and fragrance¹² of the vinegar. Pharmaceutical scientists are researching methods to measure polyphenol amounts in food and measure their antioxidant potential.¹³ Valuable instruments for measuring the antioxidant levels of different foods are being developed.¹⁰ The health benefits depend on both the intake and bioavailability of the substance.¹⁴ Several epidemiological studies have found that

polyphenols provide protection from cardiovascular disease, cancer, diabetes, infections, aging, dementia, and hypercholesterolemia.¹⁵

ETIOLOGY, EPIDEMIOLOGY, AND BASIC SCIENCE RESEARCH

Antitumor. Black vinegar or brown rice vinegar is used as a condiment in sushi and other Asian restaurants in the United States. Kurosu, traditional Japanese vinegar or black vinegar, contains ethyl acetate, which has superior antioxidative activities,^{14,16} along with polyphenols, which can inhibit the growth of human cancerous cells.^{6,14} These additional polyphenols are found in black vinegar — quercetin, catechins (also in apple cider vinegar), isoflavones, lignans, flavones, ellagic acid, resveratrol, and curcumin — and all were tested to show protective effects against cancer sites. These protective effects have been observed in cancer locations of the mouth, the stomach, the duodenum, the colon, the liver, the lung, the mammary glands, and the skin.¹⁴

Experiments conducted on rats have shown that ethyl acetate extracts of Japanese black vinegars can prevent azoxymethane-induced colon cancer by increasing enzymes in the liver that prolong the life of the rats.¹⁷ Much of the information on the health benefits of fruit vinegars has not been evaluated formally in rigorous clinical trials. However, investigations on polyphenols, especially resveratrol, have shown that the prolonged use of fruit vinegars may lead to protective anticancer outcomes in humans. Future research should focus on the analogous active ingredients of these fruit and black vinegar extracts and their role in tumor necroptosis.

Antiobesity, Anti-lipidemic. It is suggested that humans must consume at least 0.3% of acetic acid daily (1 to 2 tablespoons of vinegar in 8 ounces of water) to reduce serum cholesterol, triglycerides,¹⁸ and improve digestion.¹⁹ In 2009, Kondo et al studied 155 obese, healthy Japanese subjects who consumed a 500-mL beverage with 15 to 30 mL (1 to 2 tablespoons) apple cider vinegar for 12 weeks. They found that body mass index, visceral fat, waist-to-hip ratio, and triglycerides all decreased at both doses.²⁰ The following triglyceride levels were found: placebo group (1.71 ± 0.50 mmol/L to 1.68 ± 0.67 mmol/L), low-dose apple cider vinegar group (1.70 ± 0.60 mmol/L to 1.39 ± 0.58 mmol/L), and high-dose apple cider vinegar group (1.78 ± 0.55 mmol/L to 1.31 ± 0.54 mmol/L). The acetic acid present in vinegar may down-regulate gene expression in cholesterol synthesis or upregulate gene expression in favor of fatty acid oxidation, thus enhancing lipolysis.²¹

Beheshti et al performed another study in which 19 hyperlipidemic patients consumed 30 mL (2 tablespoons) of apple cider vinegar twice a day, and they noted

Table 2: Decreased Blood Glucose After Apple Cider Vinegar

Reference	Participants	Trial Design	Vinegar Ingestion	Meal	Intervention	Outcomes
Johnston et al. (2004)	8 healthy, 11 insulin-resistant, and 10 T2D subjects	Crossover, placebo-controlled	Acute	White bagel, butter, orange juice	20 g (4 tsp.) ACV	Decreased insulin response without effect on postprandial glucose (PPG) in healthy subjects Reduced PPG and insulin levels as well as increased insulin sensitivity in insulin-resistant subjects No effect in diabetic subjects
Johnston & Butler et al. (2005)	11 healthy subjects	Randomized, crossover, placebo-controlled	Acute	Bagel + juice (high GL) or chicken + rice (low GL)	20 g ACV	Reduction in insulin response in both meals Reduction in glucose response in high-glucose-loaded meal
Hlebowicz et al. (2007)	10 T1D subjects with gastroparesis	Crossover, investigator-blinded	Chronic (2 wk)	300 g rice pudding	200 mL water ± 30 mL ACV	Reduction in gastric emptying rates
White & Johnston (2007)	11 T2D subjects	Randomized, crossover, placebo-controlled	2 d	1 oz. cheese at bedtime	2 Tbsp. ACV at bedtime for 2d	Reduction in fasting glucose in day 2, particularly in subjects with typical fasting glucose > 7.2 mmol/L
Salbe et al. (2009)	5 healthy subjects	Randomized, crossover, placebo-controlled	Acute	Mashed potatoes, 1 Tbsp. margarine, + 120 mL sugar-free beverage	Vinegar (20 mL ACV, 40 mL water, 0.3 tsp. saccharin)	Glucose levels in the first 100 min were greater after vinegar ingestion Vinegar was unable to suppress enteral glucose absorption
Panetta et al. (2013)	97 non-diabetic patients	Parallel, randomized, double-blind, placebo-controlled	Chronic (8 wk)	Foods consumed as part of daily routine	30 mL ACV	No difference in HbA1c
Wu et al. (2013)	7 non-diabetic women with PCOS	Clinical	Chronic (90-110 d)	Foods consumed as part of daily routine	100 mL beverage containing 15 g ACV	Restoration of ovulatory function as well as a modest (statistically significant) decrease in HOMA-IR

reduced cholesterol, low-density lipoprotein (LDL), and triglycerides after eight weeks compared to baseline.²² These studies contrast with a parallel, randomized, double-blind, placebo-controlled eight-week trial on 97 non-diabetic subjects that found no significant differences in high-density lipoprotein, LDL, total cholesterol, triglycerides, or high-sensitivity C-reactive protein. Interpreting these results is difficult because some of the study participants were also taking fish oil and/or statin medications while in the study. More investigations need to be made behind the lipid-lowering potential of apple cider vinegar in carefully constructed clinical trials. Vinegar made from tomatoes has antiscerous properties, and when consumed regularly can reduce the total gut fat and the adipocyte cell size.^{23,24} Human and animal studies showed that tomato vinegar could be used as an antiobesity and antidiabetic agent^{24,25} and that consumption of acetic acid reduced serum triglycerides.²⁶

Antidiabetes. Diabetes is a worldwide public health problem.²⁷ Researchers are now looking at vinegars and other bioactive components of foods as an adjuvant treatment for diabetes. The first effect of vinegar on blood glucose levels was published in 1988. When researchers gave rats a solution of 2% acetic acid after a high-glucose meal, the blood glucose levels were reduced.²⁸ A series of human studies ensued on how blood glucose levels are reduced when fruit vinegars are taken after a high carbohydrate meal. (See Table 2.) Vinegar was ineffective in reducing postprandial blood glucose after low-carbohydrate meals,²⁹ possibly because it works on the digestion of food.³⁰ Additional research is needed in this area but apple cider vinegar may reduce glucose during digestion by delaying gastric emptying and/or through the inhibition of enzyme activity thereby influencing carbohydrate absorption.^{31,32,33}

Vinegar can decrease blood glucose after high-carbohydrate meals, increase insulin response, and increase satiety. A systematic review of randomized and non-randomized, controlled clinical trials on diabetic patients who consumed vinegar in therapeutic amounts (4 teaspoons to 2 tablespoons) found a small but significant reduction in mean HbA1c after 8-12 weeks of vinegar administration (-0.39; 95% confidence interval [CI], -0.59 to -0.18; 12: 0%). Other significant findings were a lower pooled mean difference in glucose levels at 30 minutes in the vinegar group.²⁷ Future research should use carefully planned large clinical trials on how vinegar can be used as an adjunct treatment modality for diabetes. A meta-analysis of clinical trials involving vinegar's effect on postprandial glucose and insulin responses³⁴ confirmed this recommendation.

In the last two decades, vinegar has been shown to decrease blood glucose levels in healthy and diabetic adults.³⁴ In 2017, Shishehbor et al performed a pooled analysis of 11 studies that exposed a significant mean glucose and insulin area under the curve (AUC) in participants who consumed vinegar compared with the control group (standard mean difference, - 0.60; 95% CI, - 1.08 to -0.11; $P = 0.01$; and -1.30; 95% CI, -1.98 to -0.62; $P < 0.001$, respectively).³⁵ In the two studies, patients had decreased postprandial glucose and insulin in the vinegar groups. Vinegar can improve the insulin sensitivity of humans and may be used as an adjuvant treatment.^{35,36}

SUMMARY

Vinegar is a popular subject in the literature surrounding chronic disease prevention and treatment. Inflammation has been identified as the driving force behind chronic diseases. The antioxidant properties of vinegar, fruits, vegetables, and legumes have been proven effective in the management and prevention of chronic disease.

ADVERSE EFFECTS

Apple cider vinegar remedies are advertised widely online as treatments for a variety of health problems. Everything from tablets, pills, drinks, dog rinse cleansers, and traditional vinegars are touted as cures and tonics. There have been a few cases of apple cider vinegar adverse effects in the literature. Investigators examined several types of apple cider vinegar pills on the market after an initial complaint from a patient with pain and difficulty swallowing when an apple cider vinegar tablet had lodged in her throat for 30 minutes. The safety, reliability, and quality of these supplements are in question because of unreliable and erroneous labeling techniques, dosage variability in amounts of active compounds, and the uncorroborated health benefits.³⁷ There is a risk of increased incidence of chemical burns when treating skin disorders, warts, and Mollusca

with acetic acid or vinegar.³⁸ The first case of sudden cardiac death due to forced ingestion of 5% acetic acid was published in 2016.³⁹ Individuals have experienced disseminated intravascular coagulation, requiring treatment with fresh frozen plasma and cryoprecipitate,⁴⁰ as well as hepatic abnormalities⁴¹ following the ingestion of acetic acid. It is recommended that vinegar be ingested only in dilute amounts. Many cases of corrosive injuries have taken place when vinegar is ingested undiluted.

Apple cider vinegar is highly acidic. The main ingredient is acetic acid, which can be relatively corrosive. Household vinegar, which is typically 5% acetic acid, should be diluted (1-2 tablespoons) in an 8-ounce glass of water or juice before swallowing.³⁷ Pure, straight apple cider vinegar could damage tooth enamel or the tissues of the mouth and throat.⁴² The average pH of apple cider vinegar is between 2.5 and 3.0.⁴² Long-term ingestion of excessive amounts (> 1 to 2 tablespoons in an 8-ounce glass of water) of even diluted acetic vinegar can cause low potassium levels and lower bone density.⁴³ One incident of anaphylaxis from unpasteurized apple cider vinegar (bACV) occurred in a 40-year-old female who drank 30 mL of bACV for two weeks until she developed diffuse urticaria, nausea, vomiting, abdominal pain, and difficulty breathing after the last dose and was treated in the emergency department with injected epinephrine, steroids, and diphenhydramine. A challenge with 15 mL bACV after five minutes showed progressive flushing, groin pruritus, and hives requiring epinephrine, diphenhydramine, ranitidine, and prednisone. Subsequent oral challenge to 15 mL bACV was negative. The patient was advised to avoid bACV and keep epinephrine available.⁴⁴

It has been theorized that apple cider vinegar may interact negatively with the following medications: antidiabetic medications, digoxin, diuretic drugs, and insulin.

Apple cider vinegar might have additive effects on glucose levels when used with hypoglycemic drugs. Hypothetically, overuse of apple cider vinegar could decrease potassium levels, increasing the risk of toxicity for digoxin, diuretics, and insulin. Physicians should monitor blood glucose and potassium levels closely and medication dose adjustments may be necessary.

CONCLUSION

Apple cider vinegar has antioxidant, anti-lipidemic, antidiabetic, and therapeutic properties.⁶ Apple cider vinegar is made from apples by the process of alcohol fermentation and acetous fermentation. Bioactive compounds and acetic acids are the active components in vinegar that are responsible for health benefits. The antidiabetic properties are the most promising because of the backing of several meta-analyses on clinical tri-

als supporting vinegar's ability to lower postprandial glucose and improve insulin sensitivity. Vinegar has been shown to be helpful in weight loss, decreasing postprandial glucose, and lowering lipid levels.^{21,22, 23}

RECOMMENDATION

Definitive studies on vinegar are still surfacing relative to its safety and efficacy. Advise patients to be cautious about their vinegar consumption, and limit the dose to no more than 2 tablespoons daily diluted in 4 to 8 ounces of juice. For weight loss, vinegar might work best when consumed before meals, especially those that are high in carbohydrates. With respect to types of vinegar, the best data are on apple cider vinegar, and some experts recommend organic, unfiltered, unprocessed vinegar, which is cloudy, containing the "mother," or collection of enzymes and probiotics, possibly indicating a quality product. Future clinical trial research should investigate how vinegar can be used as an adjunct treatment modality for diabetes and prevention or treatment of other chronic diseases. ■

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CME QUESTIONS

1. Which of the following is true regarding the homeopathic cough syrup used for pediatric upper respiratory infections?
 - a. It improved various functional parameters through the study period more than in the placebo group.
 - b. There was a greater improvement one hour after syrup dosage at all time points.
 - c. Compared to the placebo group, it improved symptoms such as cough, runny nose, and sneezing during the first day, but not thereafter.
 - d. There were less side effects seen in the homeopathy group.
2. In the Miller et al study regarding tea, coffee and cardiovascular health, which of the following statements is true?
 - a. Moderate consumption of green tea was associated with reduction of cardiac calcium accumulation; moderate consumption of black tea was associated with a reduction of cardiac events.
 - b. Highly caffeinated coffee consumption of more than 1 cup/day correlated with higher numbers of cardiac events.
 - c. Consumption of more than 1 cup daily of black and/or green tea was associated with reduced progression of coronary artery calcium and cardiac events.
 - d. Cardiac events appeared to be most closely associated with caffeine content of drinks, as well as the total amount of caffeine consumed daily.
3. What is the recommended dose of apple cider vinegar for your diabetic patients?
 - a. 3-4 teaspoons of apple cider vinegar with a water chaser
 - b. 1-2 teaspoons of apple cider vinegar
 - c. 1-2 tablespoons of apple cider vinegar diluted in 8 ounces of water.
 - d. 1-2 tablespoons of apple cider vinegar diluted in 4 ounces of water.

CME OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- present evidence-based clinical analyses of commonly used alternative therapies;
- make informed, evidence-based recommendations to clinicians about whether to consider using such therapies in practice; and
- describe and critique the objectives, methods, results, and conclusions of useful, current, peer-reviewed, clinical studies in alternative medicine as published in the scientific literature.

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