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Therapeutic effects of vinegar: a review

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Vinegar is a natural product derived from a process of fermentation. Carbohydrates-rich foods are excellent sources of substrate to produce vinegar. Vinegar is mainly used as an ingredient in food preparation due to its taste and aroma. It is one of the most famous folk medicines used to fight infections. Several studies have showed vinegar has a potential to ameliorate obesity, diabetes, cardiovascular disorders, cancer and microbial infections. Daily intake of a drink containing 15 mL vinegar (750 mg of acetic acid) was reported to improve lifestyle-related diseases, such as hypertension, hyperlipidemia, and obesity. The presence of acetic acid and other components in vinegar could be responsible for its therapeutic effect. This paper reviews recent studies on therapeutic values of vinegar derived from different food sources. Possible mechanisms of therapeutic action of vinegar are also discussed.

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Introduction

Vinegar is a natural food product derived from fermentation processes (alcoholic and subsequently acetous fermentation) that involve fermentable glucose in apple, dates, grape, fig, and many other carbohydrate-rich food products [1]. Historically, the production of vinegar is for medicinal purposes due to its therapeutic values. Health-promoting properties of vinegar have been traditionally known to include as an antimicrobial agent and in preventing negative health outcomes [2].

Vinegar has been used as a therapeutic agent to attenuate obesity since late 18th century. Post World War 1, anti-obesity drugs such as dinitrophenol, amphetamine, and fenfluramine started to be used but caused many health complications and side effects [3]. Thus, scientists have investigated the effectiveness of vinegar as an alternative medicine for obesity. Several studies have reported acetic acid is a bioactive compound present in vinegar that exhibits various therapeutic values. Furthermore, Cho *et al.* [4] reported that phenolic compounds (chlorogenic acid, gallic acid and caffeic acid) in vinegar could improve lipid metabolism and have antiobesity effect in obese rats. Up to date, vinegar has been reported not only for attenuating obesity [5], but also shown to exhibit therapeutic effects on diabetes [2,6], cardiovascular disorders [7] and cancer [8,9] as shown in Table 1.

One of the main ingredients in the Mediterranean diet is vinegar, and vinegar was believed to play crucial role in impeding cardiovascular disease as vinegar ingestion may diminish blood pressure [10–13]. In exerting its hypotensive action, taking vinegar may prevent the bradyarrhythmia effect, a slow heart rate symptom that can lead to fatigue, weakness, dizziness, and loss of consciousness [14]. Vinegar also possesses antioxidant capacity that may be a reliable health-promoting activity [15]. Moreover, it has been recommended that daily vinegar supplements could increase HDL-cholesterol and diminish LDL-cholesterol levels [16].

In the other case, vinegar (5%, v/v) or acetic acid (0.3%, w/v) were used in treating ulcerative colitis (UC) due to its ability in hindering inflammation through suppressing T helper 17 (Th17) and mitogen-activated protein kinase (MAPK), the pivotal signaling in pathway of UC. Supplementation of vinegar and acetic acid to dextran sulfate sodium (DSS)-induced mice reported effectively ameliorate body weight loss, shorten the colon length in a murine experimental colitis, reduce disease activity index (DAI), and histopathological scores [17].

Vinegar improves lipid profiles and suppresses fat accumulation

High dietary cholesterol will induce significant increases in liver cholesterol and triacylglyceride concentrations [18] which can lead to health complication such as atherosclerosis and hypertension. Intriguingly, vinegar supplementation is one of effective and low cost medications suggested to reduce the formation of triacylglycerides in the liver [19] by elevating hepatic glutathione (GSH) and trolox equivalent antioxidant capacity (TEAC) levels, as well as catalase (CAT) and glutathione peroxidase (GPx) activities [20].

The presence of acetic acid in vinegar will stifle sterol regulatory element-binding protein (SREBP) gene

Table 1

Health benefits of different vinegar types.

Type of vinegar	Effects	References
Persimmon vinegar	- reduce hepatic triglyceride (TG) and total cholesterol (TC) concentration - lower the acetyl-CoA carboxylase (ACC) mRNA level • Effective in reducing obesity	Moon *et al.* [21•]
Tomato vinegar	- reduced the body and visceral fat weight - lower plasma free fatty acid, triglyceride and hepatic triglyceride levels - enhance fatty acid beta-oxidation carnitine palmitoyltransferase activities - increase glucokinase activity and decreased glucose-6-phosphatase activity - lower plasma LDL-cholesterol level and elevate HDL-cholesterol • Can be used as an antiobesity and antidiabetic agent	Seo *et al.* [5] Lee *et al.* [16]
Pomegranate vinegar	- increase phosphorylation of AMP-activated protein kinase (AMPK) - decrease sterol regulatory element binding protein-1c (SREBP-1c) and peroxisome proliferator-activated receptor (PPARγ) • Attenuate adiposity through AMPK regulation	Ok *et al.* [27] Park *et al.* [28•]
Ginseng radix vinegar	- decrease insulin resistance up to 90% - inhibit weight gain - lower fasting and postprandial glucose concentrations • Ameliorate obesity and diabetes through improved lipid and glucose metabolism	Yun *et al.* [15] Lim *et al.* [30]
Nypa palm vinegar	- Its aqueous extract showed significant blood glucose lowering effect - significant improvement in serum insulin levels up to 80% • Should be taken by type 2 diabetes patient because its antihyperglycaemic effect comparable to metformin	Yusoff *et al.* [6]
Kurosu vinegar	- inhibit the proliferation of cancer cells - enhance programmed necrosis (necroptosis) in cancer cells • Possess anticancer effects against almost human cancer cells	Baba *et al.* [8] Nanda *et al.* [43]

expression in mRNA level and also reduce activity of ATP citrate lyase (ATP-CL). This process may reduce the level of pivotal substrates (acetyl-CoA and HMG-CoA) required for cholesterol and fatty acid synthesis [21••]. Acetic acid increases alternative oxidase (AOX) gene expression, thus resulting in boosting fatty acid oxidation. The study showed acetic acid not only inhibits cholesterol and fatty acid formation in liver, but also enhances lipolysis [22]. Ingestion of vinegar produced from persimmon will ameliorate blood lipid profiles through elevating body carnitine level and may promote lipid oxidation [22]. Both human and animal studies showed that the supplementation of acetic acid reduced the level of serum triacylglyerides [14,23].

As shown in Table 1, it has been demonstrated that tomato vinegar beverage (TVB) supplementation significantly reduced triglyceride and cholesterol levels in liver and also lessen plasma free fatty acid concentration [16,24••]. In addition, TVB lowered plasma LDL-cholesterol level [25], reduced the development of fatty plaques in the arteries, and increased ratio of HDL-cholesterol to total cholesterol [16,26,27]. Fecal triglyceride excretion also increased due to vinegar supplementation, indicating it helps in cholesterol flush out from the body [16,20].

Ok *et al.* [28•] have reported that supplementation of acetic acid and pomegranate vinegar (PV) contributed to lowering both plasma and hepatic triglyceride levels. Interestingly, in their study the effectiveness of PV in reducing plasma triglyceride was favored more at a low dose when compared to a high dose. This could be due to various properties of diverse chemical compounds present in PV.

Vinegar derived from pomegranate seems to be popular for obesity treatment because it has been reported to inhibit lipogenesis and enhance fatty acid beta-oxidation [28•,29]. Moreover, ingestion of PV may induce upregulation of peroxisome proliferator-activated receptor alpha (PPARα) [21••] and carnitine palmitoyltransferase 1 alpha (CPT-1a) mRNA expressions including phosphorylation of adenosine monophosphate-activated protein kinase (AMPK) better than acetic acid [28•], indicating that PV is more potent than acetic acid in attenuating obesity.

Yamashita [30] investigated possible mechanisms of vinegar in obesity attenuation. AMPK, a kinase enzyme which acts as a key metabolic master switch, and plays a pivotal role in lipid homeostasis will increase as AMP/ATP ratio increases due to vinegar supplementation. Phosphorylation of AMPK will induce PPAR-alpha gene expression [14] that regulates mRNA expression of fatty acid oxidation enzymes, such as acetyl-CoA (ACCA) oxidase and CPT-1a, which may enhance fatty acid β-oxidation. Activation of AMPK as well as down-regulation of SREBP-1c [29] and carbohydrate-responsive element-binding protein (ChREBP) expression will inhibit lipid

accumulation. AMPK also plays a vital role in lipolysis as it instigates up-regulation of hormone-sensitive lipase (HSL), resulting in the promotion of lipid breakdown [28•]. Thus, the ability to promote fatty acid oxidation, enhance lipolysis and inhibit lipogenesis suggests that vinegar can be used as natural medication for anti-obesity [2,24••].

A study reported that consistent ingestion of acetic acid may reduce fat pad weight without diminishing skeletal muscle weight [20,24••]. Kondo *et al.* [14] have reported that both high-dose (1.5% AcOH) and low-dose (0.3% AcOH) acetic acid supplementations to mice fed with high-fat diets showed significant reductions in weight, as well as mesenteric, perirenal and retroperitoneal white adipose tissue. Moreover, in their follow-up study on Japanese subjects, there was a different between high-dose (30 ml/day) and low-dose (15 ml/day) vinegar supplementation in lowering body weights, body mass index (BMI), and body fat ratio (BFR) [23].

Lee *et al.* [16] reported that tomato vinegar (TV) supplementation at a dose of 7 mL/kg/day exhibited anti-obesity significantly better than *Garcinia cambogia* (GC) fruits. Without altering energy intake, vinegar reduced visceral fat weight by obstructing preadipocyte proliferation, lipid accumulation and also diminishing epididymal adipocyte size [2,27].

Since early 19th century, ginseng root has been reported to be effective as a natural medication to ameliorate obesity. Yun *et al.* [15] compared the effect of vinegar derived from processed form of ginseng radix (ginsam, GS) and non-processed ginseng radix (GR) on body weight. In addition to acetic acid, GS also contains prosapogenin Rg3, a phytochemical that may contribute to observed anti-metabolic syndrome effect. Both GS and GC showed anti-hyperglycemia and weight loss effect [15,31] but GS significantly lowered hepatic fat accumulation better than that of GC. They assumed the effect could be due to presence of prosapogenin Rg3 in GS.

Vinegar reduces hyperglycaemia and improves insulin secretion

Many types of vinegars namely, apple cider vinegar [32], ginsam vinegar [15], and TV [24••] are capable of reducing postprandial blood glucose [33–35] and alleviating insulin resistance [2,35] as well as increase insulin production [26]. As shown in Table 1, Yusoff *et al.* [6] reported that an aqueous extract of nypa palm vinegar (NPV) significantly increased insulin serum concentration by enhancing production in beta-cells and also boosted beta-cells differentiation. Vinegar could neutralize the negative effects of streptozotocin, a chemical compound that is used to induce diabetes in rats because it destroys insulin-producing beta-cells.

Increasing postprandial blood flow rate after vinegar supplementation indicates an improvement in vascular activity and endothelial function, and eventually enhancement in insulin role during skeletal muscle metabolic activities. The promotion of insulin activity in the skeletal muscle is an indication of the capability of vinegar to increase glucose uptake, hence, attenuate insulin resistance in diabetic subjects [36•].

Several mechanisms regarding the role of vinegar and acetic acid in glycemia have been suggested. Taking vinegar may interfere with carbohydrate digestion [37•] and inhibit disaccharides from being broken down into absorbable monosaccharides [32]. In addition, acetic acid amplify glucose uptake [1,2,38] and increase glucose-6-phosphate concentration in liver and skeletal muscle which promote glycogen repletion [32]. Thus, vinegar may exert equal effectiveness with acarbose and metformin [39]. Johnston *et al.* [37•] have observed that ingestion of one tablespoon of vinegar at mealtime twice daily was able to reduce fasting blood glucose levels.

According to experiments done by Östman *et al.* [40], postprandial blood glucose concentration might be lowered in proportion to vinegar dose treatment. In contrast, Liatis *et al.* [41] have reported that the reduction of postprandial hyperglycemia can be affected by vinegar in high glycaemic index (GI) meal, not in low GI meal. The discrepancy was supported by Mitrou *et al.* [36•] who showed reduction of postprandial blood glucose concentration; however, vinegar ingestion with high and even low-GI meal exert improvement of insulin sensitivity as glucose uptake was enhanced. In other cases, 10 g vinegar was better in decreasing postprandial blood glucose than 2 g and 20 g vinegar. Time of vinegar ingestion prior to meal also influenced postprandial blood glucose concentration as 2 hours showed better improvement than 5 hours [42].

In attenuating hypertension, acetic acid may inhibit renin secretion and reduce the angiotensin I concentration [12]. Acetic acid also inhibits angiotensin-converting enzyme (ACE) [7,25,43] which reduces plasma angiotensin II level [23]. In addition, Nakamura *et al.* [11] reported acetic acid will enhance vasodilation due to inhibition of the strong vasoconstrictive angiotensin II.

Vinegar inhibits proliferation and induces apoptosis in human cancer cells

As shown in Table 1, vinegar derived from sugar cane (known as 'Kibizu'), Kurosu, vinegar derived from rice, and Izumi, a Japanese black vinegar made from unpolished rice showed anticancer properties by hindering the differentiation of human cancer cells via necroptosis and promoting apoptosis [7,8,12]. Budak *et al.* [1] reported that Kurosu treatment for various cancer cells (colon adenocarcinoma, lung carcinoma, breast adenocarcinoma, bladder carcinoma, and prostate carcinoma cells) might

inhibit cell proliferation. Vinegar ingestion was also effective in alleviating esophageal cancer [1]. Kurosu was reported to elevate expression of poly ADP ribose polymerase (PARP), enzymes involved in DNA repair and programmed cell death in human cancer cells [44]. Kibizu treatment to human leukemic exhibited nuclear segmentation and condensed chromatin, indicating the occurrence of apoptosis process [45].

Using cervical cancer cells, acetic acid from vinegar has been used as a sensitive, specific and accurate agent to detect development of human cancer cells. Five percent acetic acid was effective in differentiating malignant tissue from normal tissue as shown by histopathological examination. A study done by Limpaphayom *et al.* [46] has reported visual inspection using acetic acid (VIA) in improving cervical cancer prevention. Due to its reliable sensitivity, specificity and accuracy, Bhalang *et al.* [9] suggested the usage of 5% acetic acid in oral cancer examination. Vinegar has strong potentials in cancer diagnosis because it is cheaper and free of negative side effects when compared to toluidine blue and metachromatic dye that are normally used in cancer detection.

Vinegar as a natural disinfectant

Since Ancient Greece era, vinegar has been used generously as an antifungal and anti microbacterial due to its extreme low-pH in presence of acetic acid as main constituent [12]. Entry of acetic acid into cell membranes of microorganism leads to bacteria cell fatality. Antibacterial activity of vinegar depends on several factors including bacterial strain, temperature, pH, acetic acid concentration, and ionic strength. Acetic also was recognized as the best organic acid in eradicating *Escherichia coli* O157:H7, a foodborne pathogenic bacteria compared to other organic acids like lactic, citric, and malic acid [1].

Occurrence of denture stomatitis is closely related to the presence of *Candida albican*. Pinto *et al.* [47] have observed a decreasing amount of *C. albican* after soaking the denture in 10% vinegar solution for a night. Furthermore, Mota *et al.* [48] have reported that 4% apple cider vinegar showed fungicidal effect against *Candida spp*. after 30 min exposure. Hence, vinegar may be used as a denture cleansing agent as in effectively obstructing the inflammation of the mouth mucous membrane.

Taking advantage to bactericidal effect of acetic acid which is caused by its carboxylic acid function [49•], vinegar was suggested to be used in treating nail fungus, head lice, warts and ear infections [12]. A cellulose substance which is natural form in vinegar or better known as mother of vinegar was used in treating the burns as it inhibit the infections caused by bacteria [1]. Even mycobacteria, which possess disinfectant resistance due to the structure of their lipid-rich cell walls, can be killed by vinegar treatment. This makes vinegar a useful tool for treating infected wounds and scrofula, a tuberculosis glandular swellings [49•].

Wood vinegar is vinegar produced from wood waste. It exerts antifungal activity, but its effectiveness depends on the temperature during the pyrolysis process. The relationship between wood vinegar antifungal effectiveness and the pyrolysis temperature is directly proportional [50].

Post-harvest is one of the most crucial process in production line to ensure product quality and consumer acceptability. Without changing the taste, texture, and nutrient content, acetic acid solutions and vinegar have been used as post-harvest treatment in protecting meat [12] and lettuce [51] from *Escherichia coli*, *Salmonella typhimurium* and *Listeria monocytogene*.

For fruit post-harvest treatment, fumigation technique has been observed as the best way to avoid fruit decay caused by fungal conidia attached to the fruit surface. Undissociated acid can be obtain by vaporizing the vinegar, which enables penetration of the Conidia cell membrane; hence microbial death or growth inhibition is facilitated by the elevated cell protoplasm acidity. Fumigation of vinegar to fruit in post-harvest treatment effectively prevents fruit decay and may be potent in replacing sodium hypochlorite, a liquid sterilant [52]. Furthermore, tomatoes that have been fumigated with vinegar were observed to have increased lycopene concentration and no change in firmness and acidity [53]. On the other hand, a study by Krusong and his colleagues [54] has proved that vinegar in both liquid-phase and vapor-phase effectively diminish *Klebsiella pneumoniae* contamination on fresh coriander leaves.

Conclusion

Vinegar is a natural food which has several potential therapeutic benefits. The health-promoting components that contribute towards vinegar's health benefits could be acetic acid and other bioactive compounds. Various sources of vinegar (apple cider vinegar, PV, TV and others vinegar) have been shown to potentially alleviate obesity, diabetes, cardiovascular, cancer and other health complications. The therapeutic effect of vinegar could be due to several mechanisms of actions. Further research works are needed to support previous reports on the health benefits of vinegar, and to find out the best way of taking vinegar (form, quantity, time, substrate and other parameters) as a potential functional food product.

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