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Apple cider vinegar ameliorates hyperglycemia and hyperlipidemia in Tunisian type 2 diabetic patients

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Abstract

Diabetes mellitus (DM) is a globally growing health problem and has been considered as one of the five major causes of morbidity and mortality in many societies. Epidemiological studies showed that the application of plants and their derivates improve chronic disease symptoms such as cardiovascular disease, cancer and diabetes. One of the plant derivates is vinegar. Apple cider vinegar (ACV) as one the apple products is remarkably more regarded for its beneficial effects. In the current study, we examined the impact of ACV on some blood biochemical factors in type 2 diabetic patients. In this double-blind trial study, 46 patients with type 2 diabetes were divided in two groups. In the first group, 26 patients received 15ml of ACV with middle meal for one month. In the second group, 20 patients received water as placebo. At the beginning and end of the study, blood samples were collected and demographic informations including weight and body mass index (BMI) as well as some blood biochemical factors were evaluated. The findings of this study indicate that the fasting blood glucose (FBG ;p=0,003), weight (p=0,002), BMI (p=0,006), triglycérides (TG ; p=0,003), very low-density lipoproteins (VLDL; p=0,003) and total cholesterol to high density lipoprotein-cholesterol ratio (TC/HDL-C; p=0,03) reduced significantly in the first group while TC, low density lipoprotein- cholesterol (LDL-C) and LDL-C to HDL-C ratio did not show significant difference. In placebo group, no significant differences were observed. These results provide evidence that ACV supplementation can be beneficial in controlling blood parameters in patients with type 2 diabetes. Therefore, it use can be useful in patients with medicines.

Keywords: *Cider Vinegar, BMI, lipid profile, type 2 diabetes.*

Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by high levels of glucose in the blood due to the impaired secretion of insulin or insulin insensitivity (American Diabetes Association, 2005). DM affects approximately 4% of the population worldwide and is expected to increase by 5.4% in 2025 (S.H. Kim *et al*, 2006). DM is a pandemic disease and is one of the main threats to human health (K.M.V. Norayan, 2005). DM is associated with cardiovascular disease (CVD) risk factors such as dyslipidemia, hypertension and obesity, among others, which are established predictors of adverse cardiovascular outcome (C. Bauters *et al*, 2003; W.B. Kannel, 2001). It is now well established that type 2 diabetes (T2D) is characterized not only by changes in carbohydrate metabolism, but also by changes in the metabolism of lipids, which is defined in the literature as diabetic dyslipidemia.

Therefore, it is important to emphasize the fact that T2D may exist concurrently and/or synergistically with other systemic diseases, such as dyslipidemia, since there is a direct relationship between indices of glycemic control and plasma lipid elevation (A.D. Mooradian, 2009 ; K.R. Feigold and M.D. Siperstein, 1986). In patients with diabetes, alteration in the distribution of lipids increases the risk of atherosclerosis which is an insidious disease and it is possibly the most important risk factor for the development of cardiovascular events (M.P. Solano and R.B. Goldberg, 2006). Some studies have suggested that the progression to T2D from insulin resistance status occurs in parallel with the progression of atherosclerosis from endothelial dysfunction (W.A. Huesh *et al*, 2004). Dyslipidemia is a very common metabolic

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abnormality, which is characterized by a spectrum of quantitative and qualitative changes in serum lipids and lipoproteins (L.Wu and K.G. K.G. Parhofer, 2014). The main characteristics of dyslipidemia include high total cholesterol (TC), high triglycerides (TG), elevated low-density lipoprotein (LDL), and decreased high-density lipoprotein (HDL) (J.B. Lee *et al*, 2013). The cause of dyslipidemia may be genetic, environmental, or both. It has been suggested that lowering lipid levels intensively might immediately reduce the likelihood of cardiovascular disease events arising in diabetic patients (Y. Yamasaki *et al*, 2013). Co-administration of several antihyperglycemic drugs is usually necessary for the management of the hyperglycemia.

Currently, the available therapy for diabetes includes insulin and various oral anti-diabetic agents such as sulfonylureas, Thiazolidinediones, α-Glucosidase inhibitors etc. These drugs are used as monotherapy or in combination to achieve better glycemic control. Each of the above oral antidiabetic agents are associated with a number of serious adverse effects (D.E. Moller, 2001). Many patients do not respond adequately to the therapies. Therefore, novel antihyperglycemic agents with more efficacy and safety are needed (J.Halcox and A. Misra, 2015). Hence, antidiabetic drug discovery has shifted its focus to natural plant sources having minimal side effects. Plants have played a major role in the introduction of new therapeutic agents. In recent years, apple cider vinegar has been singled out as an especially helpful health remedy. It has been widely used in various dosage forms in alternative medicine for several conditions such as diabetes and obesity. Apple cider vinegar (ACV) is an acidic solution produced by fermenting apples. It contains vitamins, minerals and many trace elements (A.A. Banna and N.S. Kawar, 1982).

ACV improves the health and function of the vital organs of the body by preventing excessively alkaline urine. It is a strong detoxifying and purifying agent. It breaks down fatty, mucous and phlegm deposits within the body. It also oxidizes and thins the blood, which is important in preventing high blood pressure. ACV has been found to neutralize any toxic substances that enter the body. It neutralizes harmful bacteria that may be found in certain foods, promotes digestion, assimilation and elimination (C. Vijayakumar and C.E. Wolf-Hall, 2002; J. Hlebowiez *et al*, 2007). ACV is thought to be beneficial in the treatment of many diseases such as arthritis, cancer and diabetes. It is near 25 years that several in vivo and in vitro studies have analysed the effect of vinegar on glucose metabolism in healthy subjects and in subjects with diabetes mellitus (K. Ebihara and A. Nakajima, 1988 ; C.S. Johston *et al*, 2004).

This study addresses the effectiveness of ACV for lowering fasting glycemia in this randomized controlled trial and determines whether the intervention of taking ACV in combination of usual medical care lowers lipid profile in patients with type 2 diabetes.

Materials and Methods

The present study as clinical trial was performed in 2017 and the duration of tratments was one month. After elicidation the nature, the aim and the risks of present investigation, 46 type 2 diabetic patients were declared their satisfaction to participate in this study and so written consent was taken from all of them. The protocol was approved by Ethical Commitee of the the Institute of Nutrition and food Technology (Tunis, Tunisia).

For perform of this investigation, an entry and exist criteria was considered for all participant subjects. Inclusion criteria to study were 1) type 2 diabetic individuals suffering over 5 years 2) fasting blood glucose in range of 140-250mg/dl 3) age range between 40-65 years. Exclusion criteria were those patients that have vinegar intolerance, digestinal disorder, asthma disease, hepatic cirrhosis, chronic kidney disease (CKD), active proliferative diabetic retinopathy (PDR), congestive heart failure (CHF), myocardial infarction (MI) in recent 6 months and pregnant and lactating women.

It should be mentioned that all participant in this research have alone used oral hypoglycemic agents include metformin, biguanides and/or sulfonylurea which didn't changed in the type and dose of drugs during the study period.

All of the enrolled patients were randomly divided into two groups, vinegar receiving and placebo groups. The first group received daily 15 ml vinegar with middle meal for one month, without mixing with food or salad. Furthermore, they did not change their routine and physical activity until the end of the study. In the second group, patients received water as placebo.

Apple cider vinegar (ACV) was bought from Vital companies (Boumhel, Tunis, Tunisia). It was composed of 5% acetic acid and had a pH value of 2.8-3.

During the study, weekly telephone contacts were established with the patients and they reply the questions about any side effects such as nausea, reflux and serious drug interactions with other drugs. Also they were recommended in association with regular consumption of apple cider vinegar.

Demographic informations including weight and body mass index (BMI) were measured at the beginning and the end of the study. BMI was determined by dividing body weight in kilograms by the square of height in meters.

At the beginning and after 4 weeks, venous blood samples were collected from all patients and centrifuged at 3500 rpm for about 20 min for obtaining serum. Serum could be kept in -80°C refrigerator until evaluation. After serum separation, some blood biochemical factors including: fasting blood glucose (FBS), triglyceride (TG), total cholesterol (TC), low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), were evaluated. The TC, TG and HDL in plasma were determined using a timed endpoint enzymatic method with The SYNCHRON LX® System, UniCel® DxC 600/800

System. Glucose concentration was measured by an oxygen rate method employing a Beckman Coulter Oxygen electrode. The low density lipoprotein-cholesterol (LDL-C) and the very low density lipoproteins (VLDL) were calculated by the formula of W.T. Friedewald et *al*, (1972).

Statistical analysis

Data were expressed as mean±standard deviation of mean. Collected data were analyzed using one way analysis of variance (ANOVA) in Statistical Package for Social Sciences (SPSS) software using Wilcoxon t-test. Also, we used the method of independant t-test for data analysis beween two groups. Probability level of <0.05 indicates significant difference.

Results

After 30 days of treatment of apple cider vinegar in vinegar treated patients, there was a significant improvement in blood glucose Fasting levels (p=0,003) (Figure1), weight levels (p=0,002) (Figure2), body mass index levels (p=0,006) (Figure3).

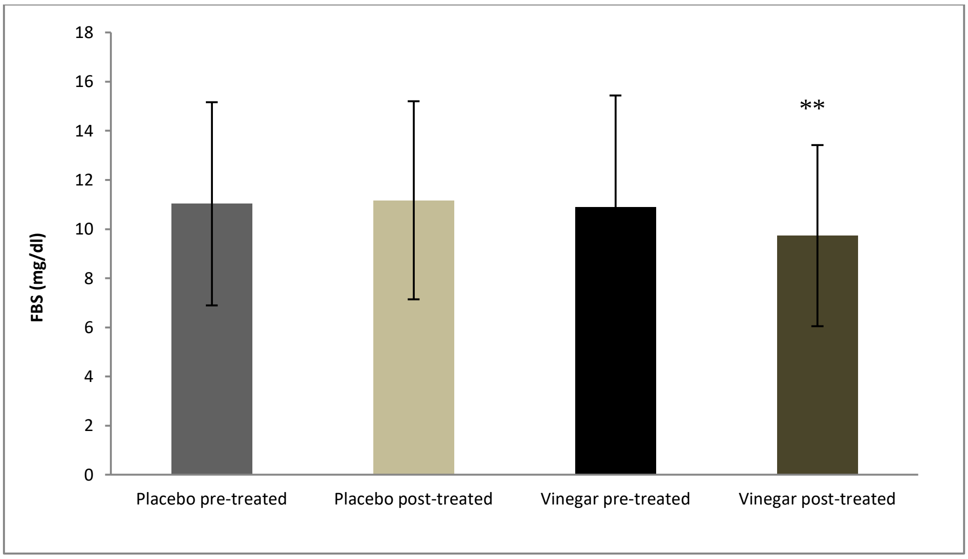

Figure 1 : Effect of apple cider vinegar on fasting blood glucose (FBS) at the beginning (pre-treatment) and the end (post-treatment) of the 30th day. Data were expressed as mean ± SD. (n=24 vinegar treated patients ; n=20 placebo treated patients), ** : p=0,003 as compared to initial values (pre-treatment). p< 0,05 is considered statistically significant.

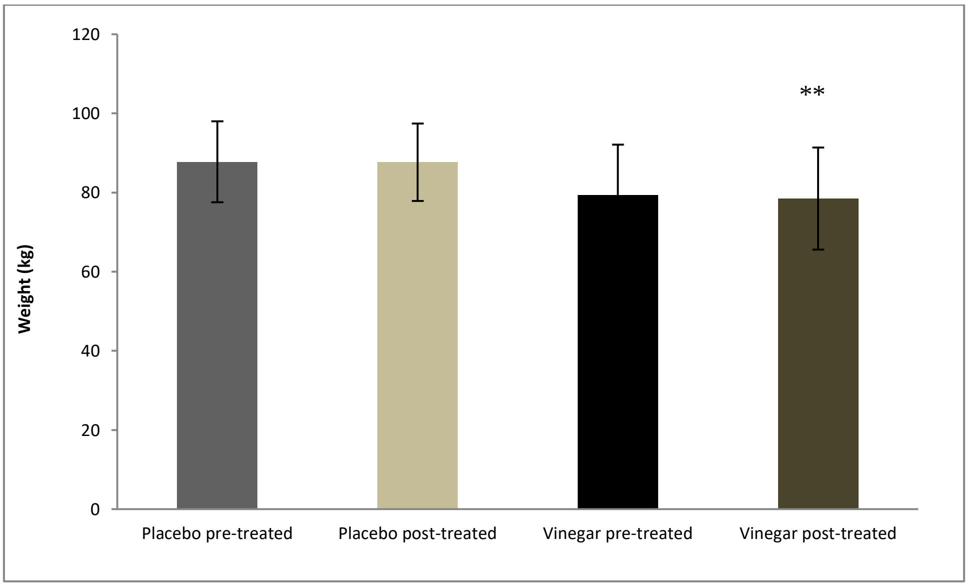

Figure 2: Effect of apple cider vinegar on body weight at the beginning (pre-treatment) and the end (post-treatment) of the 30th day. Data were expressed as mean ± SD. (n=24 vinegar treated patients ; n=20 placebo treated patients), ** : p=0,002 as compared to initial values (pre-treatment). p< 0,05 is considered statistically significant.

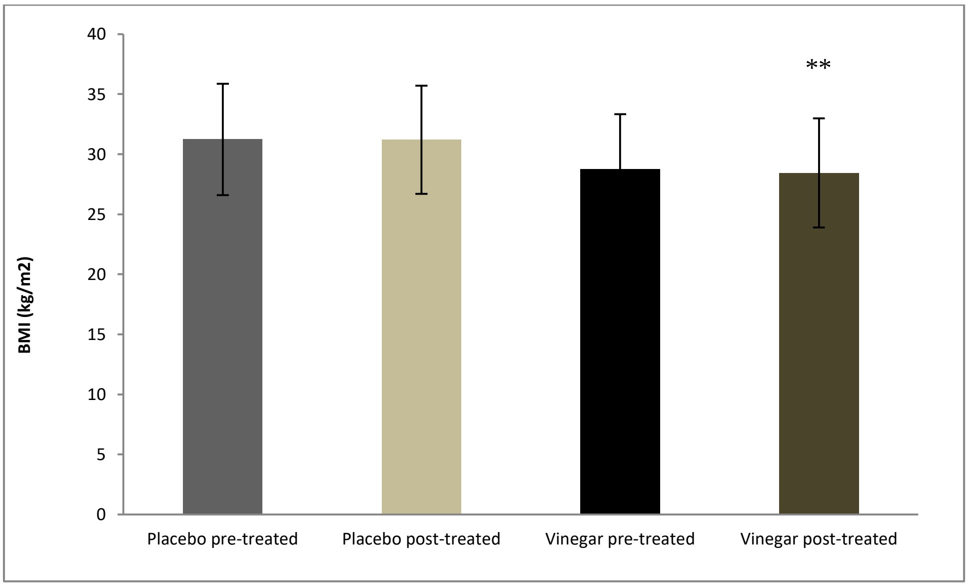

Figure 3: Effect of apple cider vinegar on body mass index (BMI) at the beginning (pre-treatment) and the end (post-treatment) of the 30th day. Data were expressed as mean ± SD. (n=24 vinegar treated patients ; n=20 placebo treated patients), ** : p=0,006 as compared to initial values (pre-treatment). p< 0,05 is considered statistically significant

Table 1 : Concentrations of serum total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL), total cholesterol to high density lipoprotein cholesterol (TC to HDL-C) ratio and low density lipoprotein cholesterol to high density lipoprotein cholesterol (LDL-C to HDL-C) ratio before and after 30 days of treatment with water (placebo treated) and apple cider vinegar (vinegar treated) in type 2 diabetic patients.

	Vinegar treated Pre-treatment	Vinegar treated Post- treatment	Placebo treated Pre-treatment	Placebo treated Post- treatment
TC (mg/dl)	4,84±1,33	4,68±1,11	4,96±0,80	5,09±0,89
TG (mg/dl)	2,11±1,43	1,81±1,04 ***	2,14±1,28	2,22±1,25
HDL-C (mg/dl)	0,99±0,14	1,08±0,23 **	0,79±0,33	0,80±0,30
LDL-C (mg/dl)	2,89±1,15	2,76±0,97	3,18±0,88	3,27±0,84
VLDL-C (mg/dl)	0,96±0,65	0,82±0,47 ***	0,97±0,58	1,01±0,57
TC/HDL-C	4,93±1,31	4,43±1,22 *	7,54±3,66	7,42±3,46
LDL-C/HDL-C	2,94±1,09	2,63±1,01	5,02±2,85	4,90±2,82

Data are expressed as Mean±SD.* :p=0,03 as compared to initial values (pre-treatment) ; ** :p=0,004 as compared to initial values (pre-treatment) ; *** : p=0,003 as compared to initial values (pre-treatment). p< 0,05 is considered statistically significant; n=24 vinegar treated patients ; n=20 placebo treated patients

Table 1 shows a significant reduction in triglyceride levels (TG ; p =0,003), very low-density lipoprotein-cholesterol levels (VLDL ; p=0,003), high-density lipoprotein-cholesterol levels (HDL-C ; p= 0,004) and Total-cholesterol (TC) to HDL-C ratio (p =0,03) when all subjects were analysed. Although there was an improvement in TC levels, low-density lipoprotein-cholesterol (LDL-C) status and LDL-C to HDL-C ratio but it was not significant (Table 1). In placebo treated group, no significant differences were observed.

Discussion

The related results for demographic informations and biochemical parameters in the first (vinegar treated) and second (water treated) groups are completely illustrated in Figure 1, Figure 2, Figure 3 and Tables 1 respectively.

Obesity is a worldwide disease affecting population of all age groups and socio-economic levels, in both developed and developing countries. It is known to be a contributory risk factor for several disease states, including diabetes mellitus (E. Al-Saleh *et al*, 2006 ; B.B. Kahn and J.S. Flier, 2000). DM is a worldwide health problem predisposing to markedly increased cardiovascular mortality and morbidity (P.Z. Zimmet *et al*, 1997). It is well-documented that increase in adipose tissue, particularly visceral adipose, is strongly associated with cardiovascular risk, moreover it has an underlying role in the development of diabetes and metabolic syndrome (A.S. Greeberg and M.L. Mc Daniel, 2002). The diabetes state itself, particularly hyperglycemia, is likely to contribute to excessive cardiovascular risk in patients with type 2 diabetes. Therefore, intensive glycemic control in DM patients may lead to overall improvement of the lipid profile of the patients and hence reduction in the associated cardiovascular risk. In this study, it was observed that vinegar significantly reduced the body weight (p=0,002) and BMI (p=0,006) in type 2 diabetic patients (Figure 2 and Figure 3). In fact, acetic acid was considered to be the active ingredient in vinegar that affected body fat reduction and body weight gain (T. Kondo *et al*, 2009). Many agents, including natural sources from traditional food, have been developed to regulate the blood fasting glucose. In this study, we examined the anti-hyperglycemic and the anti-hyperlipidemic activity of apple cider vinegar. Figure 1 demonstrates the antiglycemic properties of ACV that were firstly reported by E. Ostman et *al,* (2005) demonstrated that white vinegar reduced both postprandial blood glucose and insulin levels. In animals, at concentrations found in traditional diets, it has various effects such as enhancement of glycogen repletion (T. Fushimi *et al*, 2001). Acetic acid is the active ingredient of vinegar and several mechanisms have been suggested to explain antiglycemic effects of vinegar. It may control these factors via different manners like slowing down of gastric emptying (H. Liljeberg and I. Fjorck, 1998), inhibition of disaccharides activity in the small intestine, blocking the complete digestion of starch molecules (N. Ogawa *et al*, 2000) and also promotion of glucose uptake by muscle performance (T. Fushimi *et al*, 2006). In another study performed on human subjects, the use of a starchy meal with vinegar was reported to cause suppression of postprandial increments in serum glucose and insulin by a delayed gastric emptying rate (T. Kondo *et al*, 2009). Therefore, continuous acetic acid consumption may lead to chronically decreased serum insulin level. Several investigations examined the fact that whether delayed gastric emptying aid the hypoglycemic effects of vinegar (H. Liljeberg and I Fjork, 1998). C.S. Johnston *et al*, (2004) reported that vinegar could significantly improve insulin sensitivity in insulin resistant patients. There are some evidences that showed vinegar consumption can reduce postprandial glycaemia (E. Ostman *et al*, 2005).

In type II diabetes, insulin resistance and obesity together cause mild to moderate hypertriglyceridemia and also cause reduction of HDL-C; usually, this dyslipidemia pattern is involved with excessive production of very low density lipoproteins (VLDL). Excessive production of TG-rich lipoproteins and its low clearance by lipoprotein lipase in diabetic patients may lead to hypertriglyceridemia. TG levels inversely are associated with HDL-C, and are considered as the carrier protein for cholesterol ester in transferring cholesterol from HDL-C to VLDL. Lipoproteins in diabetic patients may also change qualitatively and quantitatively. Therefore, to reduce the risk of cardiovascular disease, many strategies have been adopted to decrease the circulating LDL-c level and increase HDL-c level (II.J. Goldberg, 2001). Apple cider vinegar has been traditionally used since many years ago to treat a certain number of diseases including hyperlipidemia which is known as a risk factor for atherosclerosis. Early prevention and treatment of atherosclerosis can prevent complications of cardiovascular diseases. The findings of this study indicate that TG (p=0,003), VLDL (p=0,003) concentrations and TC/HDL-C ratio (p=0,03) reduced significantly in the first group while TC, LDL-C and LDL-C/HDL-C ratio did not show significant difference (Table 1). T. Fushimi et *al*, (2006) observed significant reductions in TC and TG after consuming acetic acid. They reported that the acetic acid of vinegar decreased fatty acid oxidation, inhibited lipogenesis in the liver, and eventually decreased TG and TG concentrations. They recommended the impacts of acetic acid to be investigated on hamsters that are similar to humans in terms of lipid metabolism. Similarly, A. Mansouri et *al,* (2008) found that consuming apple cider vinegar 6% for four weeks improved lipid profiles of healthy and diabetic rats. M. Setorky et *al,* (2011) detected the benefits of apple cider vinegar consumption on reducing the harmful effects of a high-cholesterol diet, including atherosclerotic lesions in the aorta, among rabbits with hypercholesterolemia. They attributed the results to the influence of components, particularly flavonoids, of apple cider vinegar. There is an inverse correlation between flavonoids intake and concentration of serum total cholesterol. Since flavonoids have protective effects against atherosclerosis, their regular consumption will reduce cardiovascular disease mortality rate among elderly men (R.J. Nijveldt *et al*, 2001). This protective effect involves several mechanisms such as prevention of LDL oxidation, platelet aggregation, and improvement of endothelial functioning. Studies have indicated that flavonoids interfere with the activity of hepatocytes in the synthesis and secretion of lipoproteins containing triglyceride (R. Vidal *et al*, 2005). Epidemiologic studies have also shown an inverse relationship between the intake of dietary flavonoids and mortality caused by cardiovascular disease. The reason is the strong antioxidant properties of flavonoids that prevent LDL oxidation (N.C. Cook and S. Samman, 1996). Although an increase in serum HDL of the study subjects was observed after the intake of apple cider vinegar, this difference was statistically significant (p=0.004) (Table 1). Likewise, many other studies have reported increased HDL levels following apple cider vinegar consumptio (A. Mansouri *et al*, 2008 ; N.H. Budak *et al*, 2011). F. Shishehbor et *al,* (2007) suggested the efficacy of apple cider vinegar on modification of plasma lipoproteins, including HDL, in diabetic and healthy rats. In contrast, C.J. Panetta et *al,* (2010) evaluated the effectiveness of apple cider vinegar on increasing HDL levels. After eight weeks of consuming 30 ml vinegar daily, HDL levels were not increased compared to the control group and no evidence of beneficial properties of apple cider vinegar in controlling LDL, triglyceride, and total cholesterol was found. The difference between these studies and the present research can be due to both the type of the study subjects (animals vs. humans) and low number of participants (24 people). Hence, further studies on a larger group of people with hyperlipidemia are recommended.

Conclusion

In conclusion, the present study indicated that consumption of apple cider vinegar can reduce the LDL, triglyceride, and cholesterol levels in type 2 diabetic patients with hyperlipidemia. Besides, given that hyperlipidemia is a known risk factor for atherosclerosis, apple cider vinegar can be used to prevent and even treat this complication and probably other heart problems. However, more extensive pharmacological experiments are required.

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