Comparative Study of Tomato and Tomato Paste Supplementation on the Level of Serum Lipids and Lipoproteins Levels in Rats Fed With High Cholesterol

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Abstract

**Background:** Hypercholesterolemia is one of the risk factors of cardiovascular diseases. Increased blood cholesterol affects general health and increases mortality due to cardiovascular disease. Poor nutrition increase LDL cholesterol and decrease LDL receptor activity in the liver. Scientists have shown that consumption of antioxidants can reduce hypercholesterolemia and proved benefits of fruit and vegetables. Tomato reduces oxidative stress by increasing serum total antioxidant level.

**Objective:** This study compared the tomato and tomato paste supplementation on the level of serum lipids and lipoproteins in rats fed with high cholesterol.

**Materials and Methods:** In this study, four male rat groups (10 rats per group) were used. Control group received basal diet, second group received basal diet and 2% cholesterol (Chol), third and fourth groups received basal diet, 2% cholesterol tomato and tomato paste respectively (20 percent of the diet) for a month. Then serum TC, LDL, HDL and TG were measured.

**Results:** Results showed that in Chol group all lipids increased significantly ($P < 0.05$) except HDL compared with the control group. Tomato and tomato paste supplementation decreased TC, LDL and TG concentration significantly ($P < 0.05$) compared to Chol group. Tomato paste had the higher effect on lipids decreasing comparison with tomato.

**Conclusions:** Decreases of TC, LDL and TG may be related to tomato antioxidant effect. This course in human required more investigations.

**Key words:**

Hypercholesterolemia, Lipoproteins, Lycopersicon Esculentum, Rats
1. Background

Hyperlipidemia is the causes of half of deaths from cardiovascular diseases. Increases of blood cholesterol could treat public health (1, 2). Hypercholesterolemia is observed in most industrial societies that its main reason is poor nutrition with food containing saturated fats and high cholesterol. Poor nutrition with high cholesterol increases the cholesterol level, LDL and triglycerides levels. On the other hand hypercholesterolemia decreases LDL receptors activity in the liver. Studies showed that increases of triglyceride and cholesterol levels could decrease blood HDL level (3). Increased serum LDL level and decreased HDL level, is one of the main factors involved in cardiovascular disease, especially coronary atherosclerosis, the development that causes inflammation and reduces of endothelial function and wide vascular lesions (4). Oxidation of vessels LDL Lipoprotein, increases progression of cardiovascular disease, but increased serum HDL (unlike LDL) could prevent progress of hypercholesterolemia and cardiovascular disease (5, 6). Atherosclerosis is one of the diseases that can be caused by various factors (Multifactorial Diseases). The incidence of the disorder contributes genetic factors and environmental effects and their interaction can affect their changes. The symptoms of their interaction appear with serum lipids and lipoproteins changes, which eventually cause heart arterial diseases (1, 4, 6, 7). Studies indicate that changes in blood concentrations of lipids and lipoproteins, including triglyceride (TC), high density lipoprotein (HDL), low density lipoprotein (LDL) and total cholesterol (TC) are involved in atherosclerosis; therefore they are used in diagnosis of this type of diseases. Also it has been shown that increased serum cholesterol and LDL from one hand and decrease of HDL levels in the other hand are primary factors for predicting atherosclerosis and cardiovascular disease (1, 4, 6, 7). Results of studies have been shown that consumption of antioxidant nutrients and some foods decreases the occurrence of
cardiovascular disease due to hypercholesterolemia in humans and experimental animals (8-14). Tomatoes scientific name is Solanum lycopersicum or lycopersicon esculentum and its general name is Tomato. Nowadays tomato is used as raw or cooked into sauce and tomato paste. Compounds and substances that are involved in ripe tomato is about 80 percent water and the remaining are protein, fat, sugars including glucose and fructose, vitamins A, C, K, E, thiamin, riboflavin, pantothenic acid, folic acid, almost all essential amino acids, minerals including calcium, phosphorus, iron, sodium, potassium, magnesium, copper, manganese, cobalt, zinc, arsenic and iodine (15). Original and major color materials of tomato are carotenoid, beta-carotene and lycopene. Many pigments within fruits and vegetables have antioxidant effects, so body can use these materials to scavenging free radicals (13, 16-24). Lycopene, that causes redness color are tomatoes, is a pigment from carotenoid family. Lycopene is most abundant carotenoids found in tomatoes and ripe tomato its value increases between 10 and 14 times. Some types of carotenoids after consumption can be converted to vitamin A, but lycopene exclude of this property and form approximately 50 % of carotenoids comprise human serum. Otherwise adequate diet, the deposits decreases rapidly (13, 16-24). Studies have shown that lycopene found in tomatoes due to intensive antioxidant properties decreases the cancer risk. Tomatoes consumption prevents from pancreatic, lung, prostate and uterus cancer (21). Tomatoes consist of C and E vitamins that each of these vitamins has antioxidant properties (13, 17-19, 24, 25) In addition to materials listed above phenolic and flavonoids compounds are exist in tomato, that these compounds due to their antioxidant properties have beneficial therapy effects in many diseases (17, 22, 24-32). In traditional medicine tomato have used for the relief and improve some diseases such as asthma, cough, flu, eye diseases, ear pain, typhoid, yellow fever, colitis, arthritis (33), decreasing blood glucose and cholesterol (16, 34, 35), helping to
regulate blood pressure and reduce heart diseases (36). Several reactions in the body cause to produce peroxide, which lead to oxidize other molecules such as proteins or nucleic acids. Oxidized molecules lose their normal function and in many cases they find malicious functions. To deal with these reactions and their harmful consequences, other molecules and mechanisms that help the body defend this practice called antioxidant. Any reason that causes increases of pro-oxidant, it is called oxidative stress. In this cases the field is provide for many diseases such as cardiovascular problems following diabetes disease. Therefore it appears nutritional received antioxidant substances reduce oxidative stress, plays an important role in prevention of diabetes and cardiovascular diseases. Results of studies have shown that the Lycopene increase body antioxidants rate. Also tomato prevents LDL convert to harmful oxidized LDL and prevent arteries plaque (13, 16-24, 36, 37).

2. Objective

The aim of this study was to investigate the effect of supplementation with tomato and tomato paste on serum levels of Lipids and lipoproteins in male rats fed with high cholesterol.

3. Materials and Methods

In this study 40 male Wistar rats (for each group n = 10) were used. Weight of selected animals were 250-300 g, age 10 weeks, Animals were acclimated to the laboratory environment for 5-7 days before being used in the study. Animals were housed in a temperature and humidity controlled environment under a 12-hour light/dark cycle (lights on at 7 AM). Food and water were available ad libitum. The National Institutes of Health guidelines for care and use of animals and Guidelines on Ethical Standards for Investigation of Experimental in Animals were followed. All efforts were made to minimize the number of animals which were used and their suffering degree. Animals were randomly divided into four groups. One group as control group...
(receiving basal diet) and three subsequent dietary received cholesterol 2% ration daily for 30 days (7, 19, 38), third and fourth groups received 20% tomato and tomato paste diet daily for a month. At the end of 30 days, after a day of fasting, all animals were anesthetized by ether and then blood samples were taken from the animals. Samples were centrifuged for preparing blood serum. Total Cholesterol (TC), High Density Lipoprotein (HDL) and Triglyceride (TG), were measured by auto analyzer from isolated serum samples. Low density lipoprotein (LDL) was calculated using the Friedewald-Fredrickson formula as mg/dl \( LDL = TC - HDL - TG/5 \) (39). SPSS 13th version software used to analyze data. Group data are presented as mean ± SEM and analyzed statistically using One-Way ANOVA (ANOVA) followed by Tukey multiple comparison tests. The level for statistical significance was set at a P value of < 0.05.

4. Results

Measurement of serum TC, LDL, HDL and TG in tested groups showed that the measure of TC, LDL and TG in the group receiving dietary fat (Chol) increased significantly (P < 0.05) and the amount of HDL decreased significantly (P < 0.05) in comparison with control group (Table 1). In rats fed with high fat diet with tomato supplements (tomato + Chol) and tomato paste (tomato paste + Chol) compared with Chol group the amount of TC, LDL and TG decreased significantly (P < 0.05), but the amount of HDL increased significantly (P < 0.05), shows that there is no significant differences with control group (Table 1). Comparative study showed that tomato paste had the highest decreasing effect on lipids (Table 1).
Table 1. Effect of Supplementation with Tomato and Tomato Paste on TC, LDL, HDL and TG (mg/dl) in Serum of Male Rats Fed with High Cholesterol Diet

<table>
<thead>
<tr>
<th>Groups (n = 10), Mean ± SEM</th>
<th>TG(a)</th>
<th>HDL(a)</th>
<th>LDL(a)</th>
<th>TC(a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>45.6 ± 1.25</td>
<td>43.7 ± 1.4</td>
<td>38.2 ± 1.24</td>
<td>90.8 ± 1.85</td>
</tr>
<tr>
<td>Chol(a)</td>
<td>98.7 ± 2.1 b</td>
<td>33.2 ± 1.44 b</td>
<td>58.3 ± 1.85 b</td>
<td>112.5 ± 1.91 b</td>
</tr>
<tr>
<td>Tomato + Chol</td>
<td>52.59 ± 2.59 c</td>
<td>41.16 ± 1.3 c</td>
<td>40.22 ± 1.37 c</td>
<td>91.6 ± 1.45 c</td>
</tr>
<tr>
<td>Tomato paste + Chol</td>
<td>48.44 ± 1.75 c</td>
<td>42.78 ± 1.9 c</td>
<td>39.22 ± 1.17 c</td>
<td>90.4 ± 1.22 c</td>
</tr>
</tbody>
</table>

(a) Abbreviations: Chol, high cholesterol diet; HDL, high density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglycerides

(b) P < 0.05 compared with the control group

(c) P < 0.05 compared with Chol is in each column

5. Discussion

In this study the effect of supplementation with tomato and tomato paste on high cholesterol diet induced hyperlipidemia in male rats, were studied. Studies indicate that changes in blood concentrations of lipids and lipoproteins, including triglyceride, HDL, LDL and cholesterol are involved in atherosclerosis. It has been shown that increased serum cholesterol and LDL from one hand and decrease of HDL levels in the other hand are primary factors for predicting atherosclerosis and cardiovascular disease (1, 4, 6, 7). As the results of this study showed, adding 2 percent of cholesterol in dry matter intake for one month can alter blood lipids concentration. Adding cholesterol to rats’ diet increased the concentration of total cholesterol, LDL and TG but decreased HDL level. These results are in agreement with the results Gorinstein et al (1998) and Vaskonen et al (2002) that showed the amount of TC and LDL increased in hypercholesterolemic rats (7, 38). This model is used widely to create animal models of diet-
induced hypercholesterolemia with high cholesterol and fat. In this study, the tomato and tomato paste decreased amount of TC, LDL and TG and increased HDL levels. Various researchers have shown the effect of oral administration of this substance on blood parameters. So the results of this study conform to results of Ibrahim et al. (2008), Ali et al. in rat (17, 40). Studying of Ibrahim et al. (2008) on three different tomato products including powder, paste and tomato catchup sauce and compare their effects on body weight, lipid profiles, liver enzymes and the atherogenic index of rats reported that these three products have significantly beneficial therapeutic effects in rats and beneficial effects were most related to the tomato paste and catchup sauce relatively (40). Ali et al. (2009) showed that lycopene extracted from tomatoes is able to reduce concentrations of glucose, hydrogen peroxide, serum lipids and increase insulin concentrations, catalase, superoxide dismutase and glutathione peroxidase following the use of Streptozotocin in rats (17). Gitenay et al. (2007) showed that tomato have intensive decreasing of triglyceride levels effect and antioxidant effect compared with lycopene on oxidative stress induced by vitamin E deficiency in rats. Also tomato increases superoxide dismutase enzyme levels of red blood cells more than lycopene (26). Bobek et al. (1998) studied the effects of dried fruits apple, grape and tomato on rats, tomato decreased 15% of cholesterol and Hydroxy-Methyl-Glutaryl-CoA enzyme (HMG-CoA) but 56% increased serum antioxidant enzymes (41). Bobek (1999) also confirm previous report that dried tomato 24% reduced cholesterol, VLDL and LDL but 26% increased HDL. In liver Superoxide Dismutase enzyme activity and Glutathione Peroxidase enzyme activity increased (42). Fujiwara et al. (2007) showed that Esculeogenin A as a type of glycoside in the tomato that can decrease cholesterol, triglyceride, LDL significantly and reduce atherosclerotic lesions in ApoE (Apolipoprotein E) deficient mice. They described these effects as Cholesterol Acyltransferase protein function inhibition (43). Hsu
et al. (2008) showed that administration of tomato paste in 3-9 percent of dietary level can decrease cholesterol and LDL levels 14.3% and 11.3% respectively in the hamster. They also reported that after eight weeks of tomato paste consumption HDL level increase up to 28.8%. They subsequently reported that administration of tomato paste 89.33% decreased Malondialdehyde, and increases of Superoxide Dismutase, Catalase and Glutathione Peroxidase enzyme activity in comparison with groups received high fat diet. Their proposed mechanism on the antioxidant effect of lycopene was related to set Carbonic Anhydrase III (CAIII) and Adenylate Kinase II (AK2) (27). Unlike the above studies, Fredrikson et al. (2007) showed that lycopene can prevent the incidence of hypercholesterolemia, oxidation of plasma lipids and aortic atherosclerotic changes, 16 weeks after lycopene consumption extracted from tomato in the Watanabe Heritable hyperlipidemic rabbits (44). Several reports are presented on effect of tomato on human. Ahuja et al. (2006) have shown in a study on 21 individuals with age 70-22 years tomato lycopene compared with olive oil and showed that both compounds increased HDL and decreased cholesterol and triglyceride levels, and concluded that each compounds may decrease cardiovascular diseases due to effects on serum lipid profiles (16). Rein et al. (2006) studied on tomato flavonoids effect on some risk factors for cardiovascular disease and showed that these substances reduced C-reactive protein (CRP) and fibrinogen but in contrast increased vitamin E-selenium and serum HDL (30). Blum et al. (2006) in a study on 32 women and 16 men for one month with high tomato (300 g daily) diet showed that diet significantly increased serum HDL (15.2 %). They also reported that cholesterol, triglyceride, LDL and VLDL decreased, but these changes were not significant (34). Bose et al. (2006) showed in type II diabetic patients with long-term administration of tomato that existed lycopene reduced Glycosylated Hemoglobin (HbA1c), Malondialdehyde, Triglyceride, LDL, VLDL and
cholesterol but in contrast increases antioxidant enzymes like Superoxide Dismutase (SOD) and Glutathione Peroxidase (GSH-Px) (19). In 2007 they also confirmed previous results and reported that lycopene decreased lipid profiles except HDL, increased antioxidant levels and decreased lipid peroxidation in cardiovascular patients (45). Jacob et al. (2008) suggested that the antioxidant effect and tomato protective effects is not only because of lycopene but also in addition to ascorbic acid (vitamin C), regardless of taking the role of vitamin C, lycopene can not only was associated to tomato effects (25). Uritchard et al. (2000) studied on 57 patients with type II diabetes and showed that tomato juice increased LDL oxidation time, and decreased plasma glucose, C-reactive protein (CRP) and adhesion molecules circulation. They also based on their results suggested that the antioxidant effect is very important in myocardial infarction prevention in diabetic patients (24). Wang et al. (2006) studied on 35,783 women in the USA and reported that the uses of lycopene or lycopene-rich foods like tomatoes don’t have any relation to incidence of diseases such as diabetes type II, cancer and cardiovascular disease (46). Collins et al. (2004) also confirmed the results in middle-aged women (20). However, Basu et al. (2007) reported that tomato as lycopene source, and foods like tomato juice, tomato paste, tomato sauce and catch-up can be a source for antioxidants in the body, prevented the incidence of diseases associated with Oxidative stress. Diseases that Basu et al. mentioned are Diabetes mellitus type II, prostate cancer and cardiovascular diseases and they noted that tomato and lycopene reduces plasma lipoprotein levels, DNA damage, oxidative stress and prostate specific antigen (PSA) (18). Reboul et al. (2005) reported the beneficial effect of lycopene and tomato on prostate cancer (37). With this explanation may be differences on sexes could be realized. In summary, this study showed that supplementation with tomato and tomato paste associated with high cholesterol diet in rats, decreased the amount of TC, LDL and TG but increased HDL
concentration. These effects can be due to antioxidant and especial compounds constituents to
tomato, and probably are conducted by inhibiting lipid peroxidation and decrease production of
cholesterol, LDL and triglycerides. However, the role of tomato and tomato paste as a
supplement for the prevention of hypercholesterolemia in humans, need further investigation.

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