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The Effect of Tomato and Tomato Paste Supplementation on the Serum Lipids and Lipoproteins Levels in Rats Fed with High Cholesterol Diet

MH Khayat Nouri[1*], A Namvaran Abbasabad[2]

[1]Department of Pharmacology and Toxicology, Veterinary Faculty, Tabriz Branch, Islamic Azad University, [2]Young Researchers Club, Tabriz Branch, Islamic Azad University, Tabriz, Iran

Abstract

Background: Scientists have shown that consumption of antioxidants can reduce hypercholesterolemia including fruit and vegetables. This study aims to compare the effect of tomato and tomato paste supplementation on the level of serum lipids and lipoproteins in rats fed with high cholesterol diet.

Methods: Four groups of rats (10 male rats per group) were enrolled. Control group received basal diet, second group received basal diet and 2% cholesterol (Chol group), third and forth groups received basal diet, 2% cholesterol, tomato and tomato paste respectively (20% of the diet) for a month. Then, serum total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL) and triglyceride (TG) were measured.

Results: In Chol group, all lipids except HDL significantly increased compared with the control group. Tomato and tomato paste supplementation decreased TC, LDL and TG levels significantly compared to the Chol group. Tomato paste could decrease lipid levels more in comparison to tomato.

Conclusion: Decreases of TC, LDL and TG may be related to tomato antioxidant effects. This finding in human still requires more investigations.

Keywords: Hypercholesterolemia; Lipid; Lipoprotein; Tomato; Rat

Introduction

Hyperlipidemia is one of the main reasons of death caused by cardiovascular diseases. A high blood cholesterol is a risk factor for public health.[1,2] Hypercholesterolemia is prevalent in most industrial societies due to poor nutrition of saturated fat and high cholesterol diets increasing the cholesterol, low density lipoprotein (LDL) and triglycerides levels. On the other hand, hypercholesterolemia decreases LDL receptors activity in the liver. Many studies have shown that increases in triglyceride and cholesterol levels could decrease the blood high density lipoprotein (HDL) level.[3] Increased serum LDL level and decreased HDL level are the most important factors involved in cardiovascular diseases, especially coronary atherosclerosis leading to inflammation and reduction of endothelial function and vascular lesions.[4] Oxidation of LDL lipoprotein in vessels increases progression of cardiovascular diseases, but increase in serum HDL level (unlike LDL) could prevent progress of hypercholesterolemia and cardiovascular diseases.[5,6] Atherosclerosis is multi-factorial and its incidence contributes genetic and environmental factors leading to changes in serum lipids and lipoproteins which eventually cause cardiovascular diseases.[2,4,6,7] Some studies indicate that changes in blood levels of lipids and lipoproteins, including triglyceride (TG), HDL, LDL and total cholesterol (TC) are involved in atherosclerosis; therefore they are used in diagnosis of this kind of diseases. Also it has been shown that increased serum cholesterol and LDL from one hand and decrease in HDL levels on the other hand, are the

***Correspondence:** Mir Hadi Khayat Noori, PhD, Department of Pharmacology and Toxicology, Tabriz Branch, Islamic Azad University, Tabriz, Iran. Tel: +98-914-4137358, Fax: +98-411-5424368, e-mail: mh.khayatnouri@iaut.ac.ir

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primary factors for predicting atherosclerosis and cardiovascular diseases.[2,4,6,7]

Results of several studies showed that consumption of antioxidant nutrients and some sort of foods decreases the occurrence of cardiovascular diseases due to hypercholesterolemia in humans and experimental animals.[8-14] Tomato (*Solanum lycopersicum* or *Lycopersicon esculentum*) is nowadays used as raw or cooked forms in dressings or as tomato paste. Ripe tomato is consisted of about 80 percent water and the remainings are protein, fat, sugars including glucose and fructose, vitamins including A, C, K, E, thiamin, riboflavin, pantothenic acid, folic acid, almost all essential amino acids and minerals including calcium, phosphorus, iron, sodium, potassium, magnesium, copper, manganese, cobalt, zinc, arsenic and iodine.[15] Carotenoid, beta-carotene and lycopene are responsible for its color having antioxidant effects and are considered as scavenging free radicals.[13,16-24] Lycopene that is responsible for the red color of tomato, is a carotenoid pigment. Lycopene is the mostly abundant carotenoid found in tomato and its value is 10 to 14 times more in ripe tomato. Some types of carotenoids can be converted into vitamin A after consumption, but lycopene lacks this property and forms approximately 50% of carotenoids.[13,16-24] A study showed that the lycopene present in tomato decreases the cancer risk due to its antioxidant properties. Tomato consumption prevents pancreatic, lung, prostate and uterus cancer.[21] Tomato consists vitamin C and E that have antioxidant properties.[13,17-19,24,25] In addition, phenolic and flavonoids compounds exist in tomato with antioxidant properties that have beneficial therapeutic effects in many diseases.[17,22,24-32] In traditional medicine, tomato was used for relief of 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 reducing heart diseases.[36]

It seems that diets with antioxidant substances can reduce oxidative stress and play an important role in prevention of diabetes and cardiovascular diseases. Lycopene was shown to increase antioxidants level in the body. Also tomato was demonstrated to prevent LDL from converting to harmful oxidized LDL and preventing arterial plaques.[13,16-24,36,37] 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 a high cholesterol diet.

Materials and Methods

This experimental study was performed in fall of 2010 and 40 male Wistar rats (for each group n=10) were enrolled. Weight of selected animals were 250-300 g, age was 10 weeks and all animals were adapted 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 Experimentals 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 2%cholesterol ration daily for 30 days,[7,38] third and forth groups received 20% tomato and tomato paste diet daily for a month respectively. 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. TC, HDL and TG were measured by auto-analyzer from provided serum samples. LDL was calculated using the Friedewald-Fredrickson formula as mg/dl (LDL=TC-HDL-TG/5).[39]

SPSS software (Version 13, Chicago, IL, USA) was used to analyze data. Group data were 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.

Results

Measurement of serum TC, LDL, HDL and TG in all groups showed that 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 to the 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 ($p<0.05$), showing that no significant difference was visible in comparison to the control group

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.

Groups	TG	HDL	LDL	TC
Control	45.6±1.25	43.7±1.4	38.2±1.24	90.8±1.85
Chol	98.7±2.1[a]	33.2±1.44[a]	58.3±1.85[a]	112.5±1.91[a]
Tomato+Chol	52.59±2.59[b]	41.16±1.3[b]	40.22±1.37[b]	91.6±1.45[b]
Tomato paste+Chol	48.44±1.75[b]	42.78±1.9[b]	39.22±1.17[b]	90.4±1.22[b]

1) Group data are presented as mean±SEM (10=n for each group). 2) a: P<0.05 compared with the control group and b: P<0.05 compared with Chol is in each column. 3) Abbreviations: Chol; high cholesterol diet, TC; total cholesterol, LDL; low-density lipoprotein, HDL; high density lipoprotein, TG; triglycerides.

(Table 1). Comparative study showed that tomato paste could decrease the lipid levels more (Table 1).

Discussion

In this study, the effect of supplementation with tomato and tomato paste on high cholesterol diet hyperlipidemia in male rats was studied. Some studies indicated that changes in blood concentrations of lipids and lipoproteins, including TG, HDL, LDL and cholesterol are involved in atherosclerosis. It was shown that an increase in serum cholesterol and LDL level on one hand and decrease in HDL level on the other hand are primary factors for predicting of atherosclerosis and cardiovascular diseases.[2,4,6,7] As the results of this study showed, addition of 2 percent cholesterol in dry matter intake for one month could alter the lipid levels in the blood. Adding cholesterol to rats' diet could increase the concentration of total cholesterol, LDL and TG but decreased the HDL level. These results are in agreement with the findings of Gorinstein *et al.* (1998) and Vaskonen *et al*. (2002) showing that 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 a high fat diet. In this study, the tomato and tomato paste decreased the amount of TC, LDL and TG and increased HDL level. Various researchers have shown the effect of oral administration of this substance on blood parameters. So the results of this study confirmed the findings of Ibrahim *et al*. and Ali *et al*. in rat.[17,40] Study of Ibrahim *et al*. on three different tomato products including powder, paste and tomato catchup sauce and their effects on body weight, lipid profiles, liver enzymes and the atherogenic index of rats revealed that these three products had significantly beneficial therapeutic effects in rats and beneficial effects were most related to the tomato paste and catchup sauce relatively.[40] Ali *et al*. showed that lycopene extract from tomato could reduce the glucose, hydrogen peroxide and serum lipid levels and increase the insulin, catalase, superoxide dismutase and glutathione peroxidase levels following the use of streptozotocin in rats.[17] Gitenay *et al*. showed that tomato had an intensive decreasing effect on triglyceride level and an antioxidant effect when compared with lycopene for oxidative stress induced by vitamin E deficiency in rats. Also it was shown that tomato could increase the superoxide dismutase enzyme level of red blood cells more than lycopene.[26] Bobek *et al*. studied the effects of dried fruits of apple, grape and tomato on rats and showed that tomato was able to decrease up to 15% of cholesterol and hydroxy-methyl-glutaryl-CoA enzyme (HMG-CoA) but an increase of 56% for serum antioxidant enzymes.[41] Bobek also confirmed previous reports that reported dried tomato to reduce cholesterol, VLDL and LDL up to 24%, but increased HDL up to 26%. In liver, the activity of superoxide dismutase and glutathione peroxidase enzymes increased.[42] Fujiwara *et al*. showed that Esculeogenin A as a type of glycoside in tomato could decrease the cholesterol, TG and LDL significantly and reduce the atherosclerotic lesions in ApoE (Apolipoprotein E) deficient mice. They described these effects as cholesterol acyltransferase protein function inhibition factor.[43] Hsu *et al*. demonstrated that administration of tomato paste in 3-9 percent of dietary levels could decrease the cholesterol and LDL levels up to 14.3% and 11.3% respectively in hamster. They also reported that after eight weeks of tomato paste consumption, HDL level increased up to 28.8%. They subsequently reported that administration of tomato paste up to 89.33% could decrease the malondialdehyde, and increase the superoxide dismutase, catalase and glutathione peroxidase enzyme activities in comparison with groups received a high fat diet. The proposed

mechanism of the antioxidant effect for lycopene was shown to be related to set carbonic anhydrase III (CAIII) and adenylate kinase II (AK2).[27] Unlike the above studies, Fredrikson *et al.* showed that lycopene could 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 presented the effect of tomato in human. Ahuja *et al*. in 21 individuals aged 70-22 years showed that tomato lycopene when compared with olive oil could both increase the HDL level and decrease the cholesterol and TG levels. They concluded that each compound might decrease cardiovascular diseases due to their effects on serum lipid profile.[16] Rein *et al*. studied the effect of tomato flavonoids on some risk factors for cardiovascular diseases and showed that these substances could reduce C-reactive protein (CRP) and fibrinogen but in contrast increased the vitamin E-selenium and serum HDL levels.[30] Blum *et al*. in a study on 32 women and 16 men for one month consuming a high tomato (300 g daily) diet showed that it could significantly increase the serum HDL level (15.2%). They also reported that cholesterol, TG, LDL and VLDL decreased, but these changes were not significant.[34] Bose *et al*. in type II diabetic patients with long-term administration of tomato noticed that lycopene could reduce the glycosylated hemoglobin (HbA1c), malondialdehyde, TG, LDL, VLDL and cholesterol levels but in contrast was able to increase the 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 and increased the antioxidant levels and decreased the lipid peroxidation in cardiovascular patients.[45] Jacob *et al*. suggested that the antioxidant and protective effects of tomato were not only due to lycopene but also because of the presence of ascorbic acid (vitamin C).[25] Upritchard *et al*. studied on 57 patients with type II diabetes and showed that tomato juice increased LDL oxidation time, and decreased the plasma glucose, C-reactive protein (CRP) and adhesion molecule circulation. They suggested that the antioxidant effect was very important in prevention of myocardial infarction in diabetic patients.[24] Wang *et al*. in 35,783 women in USA reported that the use of lycopene or lycopene-rich foods like tomatoes did not have any correlation with incidence of diseases such as diabetes type II, cancer and cardiovascular diseases.[46] Collins *et al.* also confirmed the results in middle-aged women.[20] However, Basu *et al*. revealed that tomato as lycopene source, and foods like tomato juice, tomato paste, tomato sauce and catchup were a source for antioxidants in the body preventing the incidence of diseases associated with oxidative stress. Diseases that Basu *et al*. mentioned were diabetes mellitus type II, prostate cancer and cardiovascular diseases and they noted that tomato and lycopene reduced plasma lipoprotein levels, DNA damage, oxidative stress and prostate specific antigen (PSA).[18] Reboul *et al*. reported the beneficial effect of lycopene and tomato on prostate cancer.[37] With this explanation, there may be differences regarding sex. The main challenges of our study were the mixing of the diet and making sure that all rats had a high blood cholesterol level.

In summary, this study showed that supplementation of tomato and tomato pastes with a high cholesterol diet in rats was able to decrease the amount of TC, LDL and TG but increased the HDL concentration. These effects might be due to the antioxidant activity and presence of especial compounds in tomato and probably inhibiting the lipid peroxidation and decreasing production of cholesterol, LDL and TG. However, the role of tomato and tomato pastes as a supplement for the prevention of hypercholesterolemia in humans, need further investigation.

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References

1 Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA* 2001;**285**:2486-97. [113687 02] [http://dx.doi.org/10.1001/jama.285.19.2486]

2 Verschuren WM, Jacobs DR, Bloemberg BP, Kromhout D, Menotti A, Aravanis C, Blackburn H, Buzina

R, Dontas AS, Fidanza F, et al. Serum total cholesterol and long-term coronary heart disease mortality in different cultures. Twenty-five-year follow-up of the seven countries study. *JAMA* 1995;**274**:131-6. [7596000] [http://dx.doi.org/10.1001/jama.274.2.131]

3 Grundy SM, Denke MA. Dietary influences on serum lipids and lipoproteins. *J Lipid Res* 1990;**31**:1149-72. [2205699]

4 Ross R. The pathogenesis of atherosclerosis: a perspective for the 1990s. *Nature* 1993;**362**:801-9. [8479518] [http://dx.doi.org/10.1038/362801a0]

5 Devlin TM. Text book of biochemistry with clinical correlations. 3ed ed. New York: John Wiley; 1991.

6 Malloy MJ, Kane, JP. Agents used in hyperlipidemia. In: Katzung BG, editor. Basic and clinical pharmacology. 9th ed: The McGraw-Hill Companies, 2004; p. 561-75.

7 Vaskonen T, Mervaala E, Krogerus L, Karppanen H. Supplementation of plant sterols and minerals benefits obese Zucker rats fed an atherogenic diet. *J Nutr* 2002;**132**:231-7. [11823583]

8 Chorváthová V, Bobek P, Ginter E, Klvanová J. Effect of the oyster fungus on glycaemia and cholesterolaemia in rats with insulin-dependent diabetes. *Physiol Res* 1993;**42**:175-9. [8218150]

9 Fukushima M, Nakano M, Morii Y, Ohashi T, Fujiwara Y, Sonoyama K. Hepatic LDL receptor mRNA in rats is increased by dietary mushroom (Agaricus bisporus) fiber and sugar beet fiber. *J Nutr* 2000;**130**:2151-6. [10958806]

10 Hong L, Xun M, Wutong W. Anti-diabetic effect of an alpha-glucan from fruit body of maitake (Grifola frondosa) on KK-Ay mice. J Pharm Pharmacol 2007;**59**:575-82. [17430642] [http://dx.doi.org/10.1211/jpp.59.4.0013]

11 Hu SH, Liang ZC, Chia YC, Lien JL, Chen KS, Lee MY, Wang JC. Antihyperlipidemic and antioxidant effects of extracts from Pleurotus citrinopileatus. *J Agric Food Chem* 2006;**54**:2103-10. [16536582] [http://dx.doi.org/10.1021/jf052890d]

12 Kabir Y, Yamaguchi M, Kimura S. Effect of shiitake (Lentinus edodes) and maitake (Grifola frondosa) mushrooms on blood pressure and plasma lipids of spontaneously hypertensive rats. *J Nutr Sci Vitaminol (Tokyo)* 1987;**33**:341-6. [3443885] [http://dx.doi.org/10.3177/jnsv.33.341]

13 Wang HX, Ooi VE, Ng TB, Chiu KW, Chang ST. Hypotensive and vasorelaxing activities of a lectin from the edible mushroom Tricholoma mongolicum. *Pharmacol Toxicol* 1996;**79**:318-23. [9000259] [http://dx.doi.org/10.1111/j.1600-0773.1996.tb00016.x]

14 Yoshioka Y, Tabeta R, Saitô H, Uehara N, Fukuoka F. Antitumor polysaccharides from P. ostreatus (Fr.) Quel.: isolation and structure of a beta-glucan. *Carbohydr Res* 1985;**140**:93-100. [40530] [http://dx.doi.org/10.1016/0008-6215(85)85052-7]

15 Rice RP, Rice LW, Tindall HD. Fruit and vegetable production in warm climates. London, England.: The Macmillan Press Ltd; 1994.

16 Ahuja KD, Pittaway JK, Ball MJ. Effects of olive oil and tomato lycopene combination on serum lycopene, lipid profile, and lipid oxidation. *Nutrition* 2006;**22**:259-65. [16413753] [http://dx.doi.org/10.1016/j.nut.2005.07.015]

17 Ali MM, Agha FG. Amelioration of streptozotocin-induced diabetes mellitus, oxidative stress and dyslipidemia in rats by tomato extract lycopene. *Scand J Clin Lab Invest* 2009;**69**:371-9. [19148834] [http://dx.doi.org/10.1080/00365510802658473]

18 Basu A, Imrhan V. Tomatoes versus lycopene in oxidative stress and carcinogenesis: conclusions from clinical trials. *Eur J Clin Nutr* 2007;**61**:295-303. [16929242] [http://dx.doi.org/10.1038/sj.ejcn.1602510]

19 Bose KS, Agrawal BK. Effect of long term supplementation of tomatoes (cooked) on levels of antioxidant enzymes, lipid peroxidation rate, lipid profile and glycated haemoglobin in Type 2 diabetes mellitus. *West Indian Med J* 2006;**55**:274-8. [17249316] [http://dx.doi.org/10.1590/S0043-31442006000400010]

20 Collins JK, Arjmandi BH, Claypool PL, Perkins-Veazie P, Baker RA, Clevidence BA. Lycopene from two food sources does not affect antioxidant or cholesterol status of middle-aged adults. *Nutr J* 2004;**3**:15. [15369594] [http://dx.doi.org/10.1186/1475-2891-3-15]

21 Heber D, Lu QY. Overview of mechanisms of action of lycopene. *Exp Biol Med (Maywood)* 2002;**227**:920-3. [12424335]

22 Rao AV. Lycopene, tomatoes, and the prevention of coronary heart disease. *Exp Biol Med (Maywood)* 2002;**227**:908-13. [12424333]

23 Silaste ML, Alfthan G, Aro A, Kesäniemi YA, Hörkkö S. Tomato juice decreases LDL cholesterol levels and increases LDL resistance to oxidation. *Br J Nutr* 2007;**98**:1251-8. [17617941] [http://dx.doi.org/10.1017/S0007114507787445]

24 Upritchard JE, Sutherland WH, Mann JI. Effect of supplementation with tomato juice, vitamin E, and vitamin C on LDL oxidation and products of inflammatory activity in type 2 diabetes. *Diabetes Care* 2000;**23**:733-8. [10840987] [http://dx.doi.org/10.2337/diacare.23.6.733]

25 Jacob K, Periago MJ, Bohm V, Berruezo GR. Influence of lycopene and vitamin C from tomato juice on biomarkers of oxidative stress and inflammation. *Br J Nutr* 2008;**99**:137-46. [17640421] [http://dx.doi.org/10.1017/S0007114507791894]

26 Gitenay D, Lyan B, Rambeau M, Mazur A, Rock E. Comparison of lycopene and tomato effects on biomarkers of oxidative stress in vitamin E deficient rats. *Eur J Nutr* 2007;**46**:468-75. [18026867] [http://dx.doi.org/10.1007/s00394-007-0687-2]

27 Hsu YM, Lai CH, Chang CY, Fan CT, Chen CT, Wu CH. Characterizing the lipid-lowering effects and antioxidant mechanisms of tomato paste. *Biosci Biotechnol Biochem* 2008;**72**:677-85. [18323670] [http://dx.doi.org/10.1271/bbb.70402]

28 Lean ME, Noroozi M, Kelly I, Burns J, Talwar D, Sattar N, Crozier A. Dietary flavonols protect diabetic human lymphocytes against oxidative damage to DNA. *Diabetes* 1999;**48**:176-81. [9892240] [http://dx.doi.org/10.2337/diabetes.48.1.176]

29 Noroozi M, Burns J, Crozier A, Kelly IE, Lean ME. Prediction of dietary flavonol consumption from fasting plasma concentration or urinary excretion. *Eur J Clin Nutr* 2000;**54**:143-9. [10694785] [http://dx.doi.org/10.1038/sj.ejcn.1600908]

30 Rein D, Schijlen E, Kooistra T, Herbers K, Verschuren L, Hall R, Sonnewald U, Bovy A, Kleemann R. Transgenic flavonoid tomato intake reduces C-reactive protein in human C-reactive protein transgenic mice more than wild-type tomato. *J Nutr* 2006;**136**:2331-7. [16920850]

31 Saxena R, Venkaiah K, Anitha P, Venu L, Raghunath M. Antioxidant activity of commonly consumed plant foods of India: contribution of their phenolic content. *Int J Food Sci Nutr* 2007;**58**:250-60. [17566887] [http://dx.doi.org/10.1080/09637480601121953]

32 Shen YC, Chen SL, Wang CK. Contribution of tomato phenolics to antioxidation and down-regulation of blood lipids. *J Agric Food Chem* 2007;**55**:6475-81. [17629300] [http://dx.doi.org/10.1021/jf070799z]

33 Lazarus SA, Bowen K, Garg ML. Tomato juice and platelet aggregation in type 2 diabetes. *JAMA* 2004;**292**:805-6. [15315994] [http://dx.doi.org/10.1001/jama.292.7.805]

34 Blum A, Merei M, Karem A, Blum N, Ben-Arzi S, Wirsansky I, Khazim K. Effects of tomatoes on the lipid profile. *Clin Invest Med* 2006; **29**:298-300. [17144439]

35 Kordella T. You say tomato..same blood glucose, different A1Cs. Research profile. Stuart A Chalew, MD. *Diabetes Forecast* 2005;**58**:73-5. [15920813]

36 Tomato juice may protect against heart disease. *Health News* 2005; **11**:7. [15803570]

37 Reboul E, Borel P, Mikail C, Abou L, Charbonnier M, Caris-Veyrat C, Goupy P, Portugal H, Lairon D, Amiot MJ. Enrichment of tomato paste with 6% tomato peel increases lycopene and beta-carotene bioavailability in men. *J Nutr* 2005;**135**:790-4. [15795436]

38 Gorinstein S, Bartnikowska E, Kulasek G, Zemser M, Trakhtenberg S. Dietary persimmon improves lipid metabolism in rats fed diets containing cholesterol. *J Nutr* 1998; **128**:2023-7. [9808659]

39 Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* 1972;**18**:499-502. [4337382]

40 Ibrahim HS, Ahmed LA, El-din MM. The functional role of some tomato products on lipid profile and liver function in adult rats. *J Med Food* 2008;**11**:551-9. [18800906] [http://dx.doi.org/10.1089/jmf.2007.0517]

41 Bobek P, Ozdín L, Hromadová M. The effect of dried tomato, grape and apple pomace on the cholesterol metabolism and antioxidative enzymatic system in rats with hypercholesterolemia. *Nahrung* 1998;**42**:317-20. [9829269] [http://dx.doi.org/10.1002/(SICI)1521-3803(199810)42:05<317::AID-FOOD317>3.0.CO;2-Y]

42 Bobek P. Dietary tomato and grape pomace in rats: effect on lipids in serum and liver, and on antioxidant status. *Br J Biomed Sci* 1999; **56**:109-13. [10695051]

43 Fujiwara Y, Kiyota N, Hori M, Matsushita S, Iijima Y, Aoki K, Shibata D, Takeya M, Ikeda T, Nohara T, Nagai R. Esculeogenin A, a new tomato sapogenol, ameliorates hyperlipidemia and atherosclerosis in ApoE-deficient mice by inhibiting ACAT. *Arterioscler Thromb Vasc Biol* 2007;**27**:2400-6. [17872457] [http://dx.doi.org/10.1161/ATVBAHA.107.147405]

44 Frederiksen H, Rasmussen SE, Schrøder M, Bysted A, Jakobsen J, Frandsen H, Ravn-Haren G, Mortensen A. Dietary supplementation with an extract of lycopene-rich tomatoes does not reduce atherosclerosis in Watanabe Heritable Hyperlipidemic rabbits. *Br J Nutr* 2007;**97**:6-10. [17217554] [http://dx.doi.org/10.1017/S000711450721 0153]

45 Bose KS, Agrawal BK. Effect of lycopene from cooked tomatoes on serum antioxidant enzymes, lipid peroxidation rate and lipid profile in coronary heart disease. *Singapore Med J* 2007;**48**:415-20. [17453080]

46 Wang L, Liu S, Manson JE, Gaziano JM, Buring JE, Sesso HD. The consumption of lycopene and tomato-based food products is not associated with the risk of type 2 diabetes in women. *J Nutr* 2006; **136**:620-5. [16484534]