

Summary of Research Lipids 2014

Disease: Endpoints of Interest	First Author	Study Title and Complete Citation	Date	Abstract	Study Type
CVD: lipids	Sakamoto H	Elevation of serum carotenoids after continual ingestion of tomato juice. Sakamoto H, Mori H, Ojima F, Ishiguro Y, Arimoto S, Imae Y, Ogawa NT, and Fukuba H J Jpn Soc Nutr Food Sci, 47 (1994), pp. 93-99.	1994	The concentrations of lycopene and β -carotene in human serum were measured before and after continual ingestion of tomato juice. The change in the level of cholesterol during this period was investigated simultaneously. Sixty-five female students were divided into 4 groups. They ingested either 1, 2 or 3 cans of tomato juice per day and the control group received a can of apple juice per day for 4 weeks. The lycopene level in serum showed a significant increase following the ingestion of tomato juice. In the case of subjects ingesting 2 or 3 cans daily, the level in serum increased to over three times the level of serum lycopene determined at the start of the experiment. Although the β -carotene content of the tomato juice was about one-thirtieth that of lycopene, the β -carotene level in serum was about double in the subjects who ingested 3 cans daily. These results suggest that continual ingestion of tomato juice is effective for raising the serum levels of lycopene and β -carotene. Although most of the lycopene in the tomato juice was the all-trans type, a large amount of the cis-isomer was detected in the serum of the subjects after tomato juice ingestion. This would be due mainly to the isomerization reaction in the body. No significant changes in the levels of serum lipids, such as LDL-cholesterol, were observed. This suggests that the increase in the level of carotenoid in serum by ingesting tomato juice dose not induce an increase in the level of serum lipid.	RCT
CVD: lipids	Fuhrman B	Hypocholesterolemic effect of lycopene and beta-carotene is related to suppression of cholesterol synthesis and augmentation of LDL receptor activity in macrophages. Fuhrman B, Elis A, Aviram M. Biochem Biophys Res	1997	Beta-Carotene and lycopene are derived from plants, and they share similar initial synthetic pathway with cholesterol, which is synthesized in animal but not in plant cells. Thus, we sought to analyze the effect of carotenoids on macrophage cholesterol metabolism, in comparison to the effect of LDL cholesterol and of the cholesterol synthesis inhibitor, fluvastatin. In J-774 A. 1 macrophage cell line, the cellular cholesterol synthesis from [3H]-acetate, but not from [14C] mevalonate, was suppressed by 63% any by 73% following cell incubation with beta-carotene or lycopene (10 microM) respectively, in comparison to a 90% and 91% inhibition by LDL (100 micrograms of cholesterol), or by fluvastatin (10 micrograms/ml) respectively. However, unlike LDL derived cholesterol, which also suppresses macrophage LDL receptor activity, lycopene and beta-carotene augmented the activity of the macrophage LDL receptor, similarly to the effect of fluvastatin. In agreement with these in vitro observations, dietary supplementation of tomato's lycopene (60 mg/day) to 6 males for a 3 months period	Interv

		Commun. 1997 Apr 28;233(3):658-62.		resulted in a significant 14% reduction in their plasma LDL cholesterol concentrations. We thus conclude that dietary supplementation of carotenoids may act as moderate hypocholesterolemic agents, secondary to their inhibitory effect on macrophage 3-hydroxy-3-methyl glutaryl coenzyme A (HMGCoA) reductase, the rate limiting enzyme in cholesterol synthesis.	
CVD: oxidation lipids	Agarwal S	Tomato lycopene and low density lipoprotein oxidation: a human dietary intervention study. Agarwal S, Rao AV. Lipids. 1998 Oct;33(10):981-4.	1998	Increase in low density lipoprotein (LDL) oxidation is hypothesized to be causally associated with increasing risk of atherosclerosis and coronary heart disease. In recent epidemiological studies, tissue and serum levels of lycopene, a carotenoid available from tomatoes, have been found to be inversely related to risk of coronary heart disease. A study was undertaken to investigate the effect of dietary supplementation of lycopene on LDL oxidation in 19 healthy human subjects. Dietary lycopene was provided using tomato juice, spaghetti sauce, and tomato oleoresin for a period of 1 wk each. Blood samples were collected at the end of each treatment. Serum lycopene was extracted and measured by high-performance liquid chromatography using an absorbance detector. Serum LDL was isolated by precipitation with buffered heparin, and thiobarbituric acid-reactive substances (TBARS) and conjugated dienes (CD) were measured to estimate LDL oxidation. Both methods, to measure LDL oxidation LDL-TBARS and LDL-CD, were in good agreement with each other. Dietary supplementation of lycopene significantly increased serum lycopene levels by at least twofold. Although there was no change in serum cholesterol levels (total, LDL, or high-density lipoprotein), serum lipid peroxidation and LDL oxidation were significantly decreased. These results may have relevance for decreasing the risk for coronary heart disease.	Interv
CVD: lipids	Böhm V	Intestinal absorption of lycopene from different matrices and interactions to other carotenoids, the lipid status, and the antioxidant capacity of human plasma. Böhm V, Bitsch R. Eur J Nutr. 1999 Jun;38(3):118-25.	1999	BACKGROUND: The bioavailability of carotenoids has been investigated in animal studies as well as in human studies, so far mostly for beta-carotene. Only few results exist for lycopene. In recent studies, lycopene was significantly better available from processed tomatoes compared to raw tomatoes, when using daily intakes between 16.5 mg and 75 mg lycopene. AIM OF THE STUDY: In a comparative study the availability of a low oral lycopene dosage of 5 mg/d from different food matrices versus soft gel capsules containing tomato oleoresin was assessed. In addition to the plasma carotenoid content, the effect of lycopene ingestion on other plasma carotenoids, the lipid status parameters, and the antioxidant activity was estimated. METHODS: Twenty-two female adults (20-27 y) were randomized in three groups and were advised to minimize their carotenoid intake for two weeks. After this initial period, two groups received a portion of tomatoes or tomato juice adjusted to a lycopene dose of 5 mg/d, the third group ingested the same dose comprised in soft gel capsules containing tomato oleoresin. During the test period of 6 weeks, the participants continued reducing the intake of carotenoids from food. Fasting blood samples were withdrawn prior to the study, before	RCT

				<p>supplementation started, and then weekly while supplemented. Seven-day dietary records were prepared before the study started and after one week of supplementation. Carotenoids were analyzed by reversed phase HPLC with diode array detection. Dietary records were evaluated using the computer software EBIS 2.1. The plasma total cholesterol, HDL cholesterol, and triglycerides were determined enzymatically. In addition, the antioxidant activity of plasma was estimated by using the TEAC and the TRAP assays.</p> <p>RESULTS: The basal levels of lycopene in plasma were comparable for all groups (0.2-0.3 $\mu\text{mol/l}$) and decreased significantly during the two weeks of depletion to approximately 50% of the basal values. Other plasma carotenoids such as beta-carotene and beta-cryptoxanthin decreased significantly, too, whereas lutein and zeaxanthin remained unchanged. After supplementation with tomato oleoresin capsules or tomato juice, the plasma lycopene increased significantly, while it remained unchanged during intake of tomatoes. Normal dietary habits were practised of all volunteers before and during the study except vitamin C whose intake was significantly lower during the study period, because the probands were recommended to reduce the intake of fruits and vegetables. Lycopene supplementation did not affect the lipid status parameters of the three groups. After ingestion of lycopene the antioxidant activity of the plasma was not altered. Mean TEAC values were estimated to 0.33 +/- 0.05 mmol/l and TRAP values to 1.0 +/- 0.1 mmol/l and showed no significant differences in all groups during the whole study period.</p> <p>CONCLUSIONS: The bioavailability of lycopene varied significantly depending on the administered matrix. Lycopene from tomato oleoresin capsules and tomato juice (processed tomatoes) was better absorbed from the intestine than lycopene from raw tomatoes. The daily intake of 5 mg lycopene, an intake comparable to the usual daily carotenoid intake, did not affect cholesterol and triglycerides in plasma or its antioxidant capacity.</p>	
CVD: oxidation lipids	Ahuja KD	Effects of two lipid-lowering, carotenoid-controlled diets on the oxidative modification of low-density lipoproteins in free-living humans. Ahuja KD, Ashton EL, Ball MJ. Clin Sci (Lond). 2003 Sep;105(3):355-61.	2003	This study compares the effects of two lipid-lowering diets [a diet enriched in MUFAs (monounsaturated fatty acids) and a HCLF (high-carbohydrate/low-fat) diet] with a controlled carotenoid content on risk factors for coronary heart disease, including in vitro copper-induced LDL (low-density lipoprotein) oxidation and serum lipid levels. A randomized crossover dietary intervention study, with two diets each consumed for 14-16 days, was conducted in 18 women and 13 men aged 20-70 years, recruited via personal contacts and advertisements in newspapers. Both diets (MUFA-enriched diet and HCLF diet) contained the same basic foods and had a controlled carotenoid content, high in lycopene. The in vitro copper-induced oxidation of isolated LDL showed a longer lag phase (mean difference 7.4 min in women and 7.34 min in men) after the MUFA-enriched diet compared with the HCLF diet. Serum total cholesterol, LDL cholesterol and carotenoid levels were similar after the two diets. Serum triacylglycerol levels were significantly lower and those of HDL (high-density lipoprotein) cholesterol were significantly higher at the end of the MUFA-enriched diet	Interv

				<p>compared with the HCLF diet. It is concluded that the significantly longer lag phase for oxidation of LDL, the higher HDL cholesterol level and the lower triacylglycerol level in subjects following a carotenoid-controlled, MUFA-enriched diet may decrease the risk of coronary heart disease.</p>	
CVD: oxidation lipids	Kiokias S	<p>Dietary supplementation with a natural carotenoid mixture decreases oxidative stress.</p> <p>Kiokias S, Gordon MH.</p> <p>Eur J Clin Nutr. 2003 Sep;57(9):1135-40.</p>	2003	<p>OBJECTIVE: To determine whether dietary supplementation with a natural carotenoid mixture counteracts the enhancement of oxidative stress induced by consumption of fish oil.</p> <p>DESIGN: A randomised double-blind crossover dietary intervention.</p> <p>SETTING: Hugh Sinclair Unit of Human Nutrition, School of Food Biosciences, The University of Reading, Whiteknights PO Box 226, Reading RG6 6AP, UK.</p> <p>SUBJECTS AND INTERVENTION: A total of 32 free-living healthy nonsmoking volunteers were recruited by posters and e-mails in The University of Reading. One volunteer withdrew during the study. The volunteers consumed a daily supplement comprising capsules containing fish oil (4 x 1 g) or fish oil (4 x 1 g) containing a natural carotenoid mixture (4 x 7.6 mg) for 3 weeks in a randomised crossover design separated by a 12 week washout phase. The carotenoid mixture provided a daily intake of beta-carotene (6.0 mg), alpha-carotene (1.4 mg), lycopene (4.5 mg), bixin (11.7 mg), lutein (4.4 mg) and paprika carotenoids (2.2 mg). Blood and urine samples were collected on days 0 and 21 of each dietary period.</p> <p>RESULTS: The carotenoid mixture reduced the fall in ex vivo oxidative stability of low-density lipoprotein (LDL) induced by the fish oil (P=0.045) and it reduced the extent of DNA damage assessed by the concentration of 8-hydroxy-2'-deoxyguanosine in urine (P=0.005). There was no effect on the oxidative stability of plasma ex vivo assessed by the oxygen radical absorbance capacity test. beta-Carotene, alpha-carotene, lycopene and lutein were increased in the plasma of subjects consuming the carotenoid mixture. Plasma triglyceride levels were reduced significantly more than the reduction for the fish oil control (P=0.035), but total cholesterol, HDL and LDL levels were not significantly changed by the consumption of the carotenoid mixture.</p>	RCT
CVD: oxidation lipids	Collins JK	<p>Lycopene from two food sources does not affect antioxidant or cholesterol status of middle-aged adults.</p> <p>Collins JK, Arjmandi BH, Claypool PL, Perkins-Veazie</p>	2004	<p>BACKGROUND: Epidemiological studies have reported associations between reduced cardiovascular disease and diets rich in tomato and/or lycopene. Intervention studies have shown that lycopene-containing foods may reduce cholesterol levels and lipid peroxidation, factors implicated in the initiation of cardiovascular disease. The objective of this study was to determine whether consumption of lycopene rich foods conferred cardiovascular protection to middle-aged adults as indicated by plasma lipid concentrations and measures of ex vivo antioxidants.</p>	RCT

		P, Baker RA, Clevidence BA. Nutr J. 2004 Sep 15;3:15.		<p>METHODS: Ten healthy men and women consumed a low lycopene diet with no added lycopene (control treatment) or supplemented with watermelon or tomato juice each containing 20 mg lycopene. Subjects consumed each treatment for three weeks in a crossover design. Plasma, collected weekly was analyzed for total cholesterol, high density lipoprotein cholesterol (HDL-C) and triglyceride concentrations and for the antioxidant biomarkers of malondialdehyde formation products (MDA), plasma glutathione peroxidase (GPX) and ferric reducing ability of plasma (FRAP). Data were analyzed using Proc Mixed Procedure and associations between antioxidant and lipid measures were identified by Pearson's product moment correlation analysis.</p> <p>RESULTS: Compared to the control diet, the lycopene-containing foods did not affect plasma lipid concentrations or antioxidant biomarkers. Women had higher total cholesterol, HDL-C and triglyceride concentrations than did the men. Total cholesterol was positively correlated to MDA and FRAP while HDL-C was positively correlated to MDA and GPX. GPX was negatively correlated to triglyceride concentration.</p> <p>CONCLUSIONS: The inclusion of watermelon or tomato juice containing 20 mg lycopene did not affect plasma lipid concentrations or antioxidant status of healthy subjects. However, plasma cholesterol levels impacted the results of MDA and FRAP antioxidant tests.</p>	
CVD: oxidation lipids	Ahuja KD	<p>Effects of olive oil and tomato lycopene combination on serum lycopene, lipid profile, and lipid oxidation.</p> <p>Ahuja KD, Pittaway JK, Ball MJ. Nutrition. 2006 Mar;22(3):259-65. Epub 2006 Jan 18.</p>	2006	<p>OBJECTIVE: We compared the effect of two diets (a diet high in olive oil and a diet high in carbohydrate and low in olive oil) with high lycopene content and other controlled carotenoids on serum lycopene, lipids, and in vitro oxidation.</p> <p>METHODS: This was a randomized crossover dietary intervention study carried out in Launceston, Tasmania, Australia in healthy free-living individuals. Twenty-one healthy subjects who were 22 to 70 y old were recruited by advertisements in newspapers and a university newsletter. A randomized dietary intervention was done with two diets of 10 d each. One diet was high in olive oil and the other was high in carbohydrate and low in olive oil; the two diets contained the same basic foods and a controlled carotenoid content high in lycopene.</p> <p>RESULTS: Significant increases ($P < 0.001$) in serum lycopene concentration on both diets were to similar final concentrations. Higher serum high-density lipoprotein cholesterol ($P < 0.01$), lower ratio of total cholesterol to high-density lipoprotein ($P < 0.01$), and lower triacylglycerols ($P < 0.05$) occurred after the olive oil diet compared with the high-carbohydrate, low-fat diet. There was no difference in total antioxidant status and susceptibility of serum lipids to oxidation.</p> <p>CONCLUSIONS: Serum lycopene level changes with dietary lycopene intake irrespective of</p>	Interv

				the amount of fat intake. However, a diet high in olive oil and rich in lycopene may decrease the risk of coronary heart disease by improving the serum lipid profile compared with a high-carbohydrate, low-fat, lycopene-rich diet.	
CVD: lipids	Blum A	Effects of tomatoes on the lipid profile. Blum A, Merei M, Karem A, Blum N, Ben-Arzi S, Wirsansky I, Khazim K. Clin Invest Med. 2006 Oct;29(5):298-300.	2006	<p>PURPOSE: The Mediterranean diet has been reported to reduce cardiovascular mortality and morbidity considerably. Tomatoes and lycopene are considered potent antioxidants. Our purpose was to study the effects of a tomatoe-rich diet on the lipid profile following 300g daily of tomatoes for one month.</p> <p>METHODS: Plasma concentrations of triglyceride, total cholesterol, HDL-cholesterol, LDL-cholesterol and VLDL-cholesterol were determined in 98 apparently healthy volunteers (mean age 45.5+/-14.1 yr) before and after one month of follow-up. Fifty volunteers (34 women and 16 men) ate tomatoes 300g daily and 48 volunteers (32 women and 16 men) continued their regular diet without eating tomatoes for a month.</p> <p>RESULTS: In the regular diet group, there were no changes in the lipid profile: triglyceride level (169.6+/-156.8 vs. 147.6+/-93.4mg/dl; P=0.33), total cholesterol level (198.3+/-41.2mg/dl vs. 204.2+/-70.9mg/dl; P=0.23), HDL-cholesterol level (50.6+/-12.2mg/dl vs. 47.6+/-10.8mg/dl; P=0.79), and LDL-cholesterol level (122.7+/-39.4mg/dl vs. 120.2+/-32.2mg/dl; P=0.24) before and after the 1 month offollow-up. In the tomato-rich diet group: triglyceride level 170.8+/-85.4mg/dl to 167.4+/-99.4mg/ dl (P=0.98), total cholesterol level 207.5+/-44.3mg/ dl to 204.1+/-45.1mg/dl (P=0.68), HDL-cholesterol level 46.1+/-10.6mg/dl to 53.4+/-13.3mg/dl (P=0.03), and LDL-cholesterol level 127.7+/-41.8mg/dl to 119.1+/-41.7mg/dl (P=0.57).</p> <p>CONCLUSION: We found that tomatoes'-rich diet (300g daily for one month) increased HDL-cholesterol level significantly by 15.2% .</p>	Interv
CVD: oxidation lipids HgA1c	Bose KS	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. Bose KS, Agrawal BK. West Indian Med J. 2006 Sep;55(4):274-8.	2006	<p>The objective of the present study is to evaluate the beneficial effect of tomatoes, which are a rich source of lycopene, a relatively new carotenoid known to play an important role in human health. In this study, the lipid peroxidation rate was investigated by estimating malondialdehyde (TBARS) levels of antioxidant enzymes like SOD, GSH-Px, GR, GSH, lipid profile, which includes total cholesterol, triglycerides, high density lipoprotein, low density lipoprotein, very low density lipoprotein, and glycated haemoglobin HbA1c in (n = 40) the Type 2 diabetic group (n = 40) and an age-matched control group (n = 50). Significantly lower levels of antioxidant enzymes and very high lipid peroxidation rate in the Type 2 diabetic group were observed when compared to controls (p < 0.001). Likewise, significantly higher levels of lipid profile and glycated haemoglobin (HbA1c) in the diabetic group were observed when compared with control (p < 0.001). Long term tomato supplementation in diabetes mellitus showed a significant improvement in the levels of antioxidant enzymes and decreased lipid peroxidation rate (p < 0.001), but there were no significant changes in lipid</p>	Interv

				profile and glycated haemoglobin HbA1c levels ($p > 0.10$). These findings suggest that tomato lycopene may have considerable therapeutic potential as an antioxidant but there was no significant lipid lowering effect in Type 2 diabetes mellitus.	
CVD: oxidation lipids BP	Engelhard YN	Natural antioxidants from tomato extract reduce blood pressure in patients with grade-1 hypertension: a double-blind, placebo-controlled pilot study. Engelhard YN, Gazer B, Paran E. Am Heart J. 2006 Jan;151(1):100.	2006	<p>BACKGROUND: Treatment of hypertension (HT) can reduce the risk for cardiovascular diseases. Tomato extract contains carotenoids such as lycopene, beta carotene, and vitamin E, which are known as effective antioxidants, to inactivate free radicals, and to slow the progression of atherosclerosis. The purpose of our study was to evaluate the effect of tomato extract on systolic and diastolic blood pressure in grade-1 HT, on serum lipoproteins, plasma homocysteine, and oxidative stress markers.</p> <p>METHODS: This study is a single-blind, placebo-controlled trial. Thirty-one subject with grade-1 HT, without concomitant diseases, who required no antihypertensive or lipid-lowering drug therapy, who were recruited from primary care clinic, completed the trial. Subjects entered a 4-week placebo period, then an 8-week treatment period with tomato extract, 250 mg Lyc-O-Mato, and a 4-week control period with placebo.</p> <p>RESULTS: Systolic blood pressure decreased from 144 (SE +/- 1.1) to 134 mm Hg (SE +/- 2, $P < .001$), and diastolic blood pressure decreased from 87.4 (SE +/- 1.2) to 83.4 mm Hg (SE +/- 1.2, $P < .05$). No changes in blood pressure were demonstrated during placebo periods. Thiobarbituric acid-reactive substances, a lipid peroxidation products marker, decreased from 4.58 (SE +/- 0.27) to 3.81 nmol/mg (SE +/- 0.32, $P < .05$). No significant changes were found in lipid parameters.</p> <p>CONCLUSIONS: A short-term treatment with antioxidant-rich tomato extract can reduce blood pressure in patients with grade-1 HT, naive to drug therapy. The continuous effect of this treatment and the long-term beneficial effect on cardiovascular risk factors still need to be demonstrated.</p>	RCT
CVD: oxidation lipids	Madrid AE	[Short-term Lycopersicum esculentum consumption may increase plasma high density lipoproteins and decrease oxidative stress]. [Article in Spanish] Madrid A E, Vásquez Z D, Leyton A F, Mandiola C, Escobar F JA.	2006	<p>BACKGROUND: Tomato has a high antioxidant capacity due to its high content of vitamin C, vitamin E and lycopene that is a powerful free radical scavenger. However, the effects of tomato on plasma lipoproteins is not well known, and there is little evidence about the relationship between tomato consumption and oxidative state changes in humans.</p> <p>AIM: To assess in vivo the effects of dietary supplementation with pure concentrated tomato juice on short term changes in oxidative state and plasma lipoproteins in healthy volunteers.</p> <p>SUBJECTS AND METHODS: Seventeen healthy volunteers were studied. They received a supplement of pure tomato juice during 7 days. At baseline, at the end of the supplementation period and eight days after the end of the supplementation, a blood</p>	Interv

		<p>Rev Med Chil. 2006 Jul;134(7):855-62. Epub 2006 Aug</p> <p>29.</p>		<p>sample was drawn to measure total antioxidant capacity (TRAP), enzymatic antioxidants (catalase and superoxide dismutase), non-enzymatic antioxidants (lycopene and α-tocopherol) and plasma lipoproteins.</p> <p>RESULTS: Lycopene level increased early and significantly in comparison with basal levels (48% ; $p < 0.05$). TRAP, catalase and superoxide dismutase did not change significantly. HDL cholesterol increased significantly in 5.6+/-4.3 mg/dL ($p < 0.002$) on the second sampling period, improving the ratio cholesterol/HDL. It returned to baseline in the third period.</p> <p>CONCLUSIONS: Dietary supplementation of concentrated tomato juice significantly increases lycopene levels and HDL cholesterol. Non significant changes observed in TRAP, catalase and superoxide dismutase were observed during the supplementation period.</p>	
CVD: oxidation lipids	Misra R	<p>LycoRed as an alternative to hormone replacement therapy in lowering serum lipids and oxidative stress markers: a randomized controlled clinical trial.</p> <p>Misra R1, Mangi S, Joshi S, Mittal S, Gupta SK, Pandey RM.</p> <p>J Obstet Gynaecol Res. 2006 Jun;32(3):299-304.</p>	2006	<p>AIM: Menopause is a pro-atherogenic state with a sharp rise in the incidence of coronary artery disease. This pilot study was designed as an equivalence randomized clinical trial to explore the potential of LycoRed (containing 2000 microg lycopene) as an alternative to hormone replacement therapy (HRT) for the prevention of coronary artery disease in postmenopausal women. METHODS: Forty-one healthy postmenopausal women were randomly allocated to receive either continuous combined HRT (n = 21) or LycoRed (n = 20) for six months. Serum lipid profile, marker of lipid peroxidation (malondialdehyde), and the level of endogenous antioxidant (glutathione) were measured at the baseline, and 3 and 6 months after the intervention in both groups. RESULTS: At 6 months, HRT resulted in a significant decrease in total cholesterol (TC) level by 23.5% , low-density lipoproteins (LDL) by 19.6% , and an increase in high-density lipoproteins (HDL) by 38.9% . The LycoRed group showed similar changes in TC (-24.2%), LDL (-14.9%) and HDL (+26.1%). Triglyceride levels showed a smaller though significant increase at 6 months, but not at 3 months, in both groups. There was no significant change in the very LDL (VLDL) level in either group. Malondialdehyde levels decreased significantly by 16.3% and 13.3% , whereas glutathione levels increased significantly by 5.9% and 12.5% in HRT and LycoRed groups, respectively. CONCLUSION: Both HRT and LycoRed had a favorable effect on serum lipids and oxidative stress markers which were comparable. LycoRed can be used as an alternative to HRT to reduce the risk of atherosclerosis in postmenopausal women.</p>	RCT
CVD: oxidation lipids	Bose KS	<p>Effect of lycopene from cooked tomatoes on serum antioxidant enzymes, lipid peroxidation rate and lipid profile in coronary heart disease.</p>	2007	<p>INTRODUCTION: This present study aims to evaluate the beneficial effect of tomatoes, a rich source of lycopene, which is a relatively new carotenoid known to play an important role in human health and disease.</p> <p>METHODS: We investigated the lipid peroxidation rate by estimating malondialdehyde (MDA), levels of serum enzymes involved in antioxidant activities such as superoxide dismutase, glutathione peroxidase, glutathione reductase, reduced glutathione and lipid profile, which</p>	Interv

		<p>Bose KS, Agrawal BK.</p> <p>Singapore Med J. 2007 May;48(5):415-20.</p>		<p>includes total cholesterol, triglycerides, high density lipoprotein, low density lipoprotein and very low density lipoprotein in a coronary heart disease (CHD) group and an age-matched control group.</p> <p>RESULTS: We observed significantly lower levels of serum antioxidant enzymes and very high lipid peroxidation rate in the CHD group, when compared to the controls (p-value is less than 0.001). At the same time, we observed significantly higher levels of lipids in the CHD group, when compared to the controls (p-value is less than 0.001). 60 days of tomato supplementation in the CHD group showed a significant improvement in the levels of serum enzymes involved in antioxidant activities and decreased lipid peroxidation rate (p-value is less than 0.001), but there were no significant changes in lipid profile (p-value is greater than 0.10).</p> <p>CONCLUSION: These findings suggest that tomato lycopene may have considerable therapeutic potential as an antioxidant but may not be used as a hypolipidaemic agent in CHD.</p>	
CVD: oxidation lipids	Shen YC	<p>Contribution of tomato phenolics to antioxidation and down-regulation of blood lipids.</p> <p>Shen YC, Chen SL, Wang CK.</p> <p>J Agric Food Chem. 2007 Aug 8;55(16):6475-81. Epub 2007 Jul 13.</p>	2007	<p>This study was performed to understand the characteristics and biological activities of phenolics in tomatoes and to examine the effect of tomato on the regulation of blood lipids. Tomatoes of both big and small sizes were used fresh, after blanching, or after blanching and heating. Moreover, a human clinical trial was conducted to examine plasma antioxidation, status of blood lipids, and phenolic responses after ingestion of fresh tomato, tomato juice, and a lycopene drink. The contents of tomato phenolics were increased by 34% for small tomato and by 23% for big tomato after treatment by blanching and heating at 100 degrees C for 30 min. Tomato phenolics showed fair antioxidant activity (57-71%) and also synergistically promoted the antioxidation (81-100%) of tomato carotenoids. In the human clinical study, total antioxidant capacity and phenolic contents in plasma were increased after administration of fresh tomato and tomato juice, but no significant difference was found for lycopene drink consumption. Triglyceride levels and low-density lipoprotein cholesterol were decreased after administration of fresh tomato and tomato juice, and high-density lipoprotein cholesterol was increased.</p>	RCT
CVD: oxidation lipids	Silaste ML	<p>Tomato juice decreases LDL cholesterol levels and increases LDL resistance to oxidation.</p> <p>Silaste ML, Alfthan G, Aro A, Kesäniemi YA, Hörrkö S. Br J</p>	2007	<p>High dietary intakes of tomato products are often associated with a reduced risk of CVD, but the atheroprotective mechanisms have not been established. This study was conducted to investigate the effects of increased dietary intake of tomato products on plasma lipids and LDL oxidation. The diet intervention included a baseline period, a 3-week low tomato diet (no tomato products allowed) and a 3-week high tomato diet (400 ml tomato juice and 30 mg tomato ketchup daily). Twenty-one healthy study subjects participated in the study. Total cholesterol concentration was reduced by 5.9 (sd 10) % (P = 0.002) and LDL cholesterol concentration by 12.9 (sd 17.0) % (P = 0.0002) with the high tomato diet compared to the low</p>	RCT

		Nutr. 2007 Dec;98(6):1251-8. Epub 2007 Jul 9.		tomato diet. The changes in total and LDL cholesterol concentrations correlated significantly with the changes in serum lycopene (r 0.56, P = 0.009; r 0.60, P = 0.004, total and LDL, respectively), beta-carotene (r 0.58, P = 0.005; r 0.70, P < 0.001) and gamma-carotene concentrations (r 0.64, P = 0.002; r 0.64, P = 0.002). The level of circulating LDL to resist formation of oxidized phospholipids increased 13 % (P = 0.02) in response to the high tomato diet. In conclusion, a high dietary intake of tomato products had atheroprotective effects, it significantly reduced LDL cholesterol levels, and increased LDL resistance to oxidation in healthy normocholesterolaemic adults. These atheroprotective features associated with changes in serum lycopene, beta-carotene and gamma-carotene levels.	
CVD: oxidation lipids inflammation	Jacob K	Influence of lycopene and vitamin C from tomato juice on biomarkers of oxidative stress and inflammation. Jacob K, Periago MJ, Bahm V, Berruezo GR. Br J Nutr. 2008 Jan;99(1):137-46. Epub 2007 Jul 19.	2008	A human study was carried out to investigate whether tomato juice, rich in natural lycopene and fortified with vitamin C, is able to reduce several biomarkers of oxidative stress and inflammation and whether the effect can be attributed to lycopene, vitamin C or any other micronutrient. Following a 2-week depletion phase, volunteers were assigned randomly to ingest either tomato juice with (LC) or without (L) vitamin C fortification for 2 weeks (daily dose 20.6 mg lycopene and 45.5/435 mg vitamin C). Plasma and urine were analysed for carotenoids and vitamin C, lipid status, antioxidant capacity, thiobarbituric acid reactive substances (TBARS) and 8-epi-PGF2alpha, protein carbonyls, cytokines IL-1beta and TNFalpha and C-reactive protein (CRP). The consumption of tomato juice led to a reduction in total cholesterol levels (L: 157.6 v. 153.2 mg/dl, P = 0.008; LC: 153.4 v. 147.4 mg/dl, P = 0.002) and that of CRP (L: 315.6 v. 262.3 microg/l, P = 0.017; LC: 319.2 v. 247.1 microg/l, P = 0.001) in both groups. The vitamin C-fortified juice slightly raised the antioxidant capacity in urine and decreased TBARS in plasma and urine. All other markers were affected to a lesser extent or remained unchanged. Cholesterol reduction was correlated with lycopene uptake (P = 0.003), whereas the other effects could not be related with particular micronutrients. Any beneficial effects of tomato consumption for human health cannot be attributed only to lycopene and, as the additional supplementation with ascorbic acid indicates, a variety of antioxidants might be needed to optimize protection against chronic diseases.	RCT
CVD: oxidation lipids	Talvas J	Differential effects of lycopene consumed in tomato paste and lycopene in the form of a purified extract on target genes of cancer prostatic cells. Talvas J, Caris-Veyrat C, Guy L, Rambeau M, Lyan B, Minet-Quinard R, Lobaccaro JM, Vasson MP, Georgé S,	2010	BACKGROUND: Prospective studies indicate that tomato consumers are protected against prostate cancer. Lycopene has been hypothesized to be responsible for tomato health benefits. OBJECTIVE: Our aim was to differentiate the effects of tomato matrix from those of lycopene by using lycopene-rich red tomatoes, lycopene-free yellow tomatoes, and purified lycopene. DESIGN: Thirty healthy men (aged 50-70 y old) were randomly assigned to 2 groups after a 2-wk washout period. In a crossover design, each group consumed yellow and red tomato paste (200 g/d, which provided 0 and 16 mg lycopene, respectively) as part of their regular diet for 1 wk separated by 2 wk of washout. Then, in a parallel design, the first group	RCT

		<p>Mazur A, Rock E.</p> <p>Am J Clin Nutr. 2010 Jun;91(6):1716-24. Epub 2010 Apr 14</p>		<p>underwent supplementation with purified lycopene (16 mg/d) for 1 wk, whereas the second group received a placebo. Sera collected before and after the interventions were incubated with lymph node cancer prostate cells to measure the expression of 45 target genes.</p> <p>RESULTS: Circulating lycopene concentration increased only after consumption of red tomato paste and purified lycopene. Lipid profile, antioxidant status, prostate-specific antigen, and insulin-like growth factor I were not modified by consumption of tomato pastes and lycopene. We observed significant up-regulation of IGFBP-3 and Bax:Bcl-2 ratio and down-regulation of cyclin-D1, p53, and Nrf-2 after cell incubation with sera from men who consumed red tomato paste when compared with sera collected after the first washout period, with intermediate values for yellow tomato paste consumption. Cell incubation with sera from men who consumed purified lycopene led to significant up-regulation of IGFBP-3, c-fos, and uPAR compared with sera collected after placebo consumption.</p> <p>CONCLUSION: Dietary lycopene can affect gene expression whether or not it is included in its food matrix. This trial was registered by the French Health Ministry at http://www.sante-sports.gouv.fr as 2006-A00396-45.</p>	
CVD: oxidation lipids	Barona J	<p>A Mediterranean-style low-glycemic-load diet increases plasma carotenoids and decreases LDL oxidation in women with metabolic syndrome.</p> <p>Barona J, Jones JJ, Kopec RE, Comperatore M, Andersen C, Schwartz SJ, Lerman RH, Fernandez ML.</p> <p>J Nutr Biochem. 2011 Jul 18. [Epub ahead of print]</p>	2011	<p>Thirty-five women with metabolic syndrome and high plasma low-density lipoprotein (LDL) cholesterol (≥ 100 mg/dl) participated in a dietary intervention consisting of a Mediterranean-style low-glycemic-load diet for 12 weeks. Participants were randomly allocated to consume diet only (n=15) or diet plus a medical food containing soy protein and plant sterols (n=20). Plasma concentrations of carotenoids, lipoprotein subfractions and oxidized LDL (OxLDL) were measured. Independent of treatment, women had a significant increase in plasma lutein ($P < .0001$) and β-carotene ($P < .0001$), while plasma lycopene was reduced ($P < .05$) after 12 weeks. Low-density lipoprotein cholesterol was reduced from 138 ± 35 to 114 ± 33 mg/dl ($P < .0001$). In addition, decreases were observed in the atherogenic subfractions: large very low-density lipoprotein ($P < .05$), small LDL ($P < .00001$) and medium high-density lipoprotein ($P < .05$). Oxidized LDL was significantly reduced by 12% in both groups ($P < .01$). Changes in OxLDL were inversely correlated with plasma lutein ($r = -.478$, $P < .0001$). The data indicate that women complied with the dietary regimen by increasing fruits and vegetable intake. Decreased consumption of high-glycemic foods frequently co-consumed with lycopene-rich tomato sauce such as pasta and pizza may be responsible for the lowering of this carotenoid in plasma after 12 weeks. These results also suggest that plasma lutein concentrations may protect against oxidative stress by reducing the concentrations of OxLDL.</p>	Interv
CVD: oxidation lipids endothelial	Kim JY	<p>Effects of lycopene supplementation on oxidative stress and markers of endothelial function in</p>	2011	<p>OBJECTIVE: The objective was to determine the effects of lycopene supplementation on endothelial function assessed by reactive hyperemia peripheral arterial tonometry (RH-PAT) and oxidative stress.</p>	RCT

function BP		<p>healthy men.</p> <p>Kim JY, Paik JK, Kim OY, Park HW, Lee JH, Jang Y, Lee JH.</p> <p>Atherosclerosis. 2011 Mar;215(1):189-95. Epub 2010 Dec 9.</p>		<p>METHODS: Healthy men (n=126) were randomized to receive placebo (n=38), 6 mg (n=41), or 15 mg (n=37) lycopene daily for 8-week.</p> <p>RESULTS: Serum lycopene increased in a dose-dependent manner after 8-week supplementation (P<0.001). The 15 mg/day group had greater increase in plasma SOD activity (P=0.014) and reduction in lymphocyte DNA comet tail length (P=0.042) than the placebo group. Intragroup comparison revealed a 23% increase in RH-PAT index from baseline (1.45±0.09 vs. 1.79±0.12; P=0.032) in the 15 mg/day group after 8-week. hs-CRP, systolic blood pressure, sICAM-1 and sVCAM-1 significantly decreased, and β-carotene and LDL-particle size significantly increased only in the 15 mg/day group. Interestingly, the beneficial effect of lycopene supplementation on endothelial function (i.e., RH-PAT and sVCAM-1) were remarkable in subjects with relatively impaired endothelial cell function at initial level. Changes in RH-PAT index correlated with SOD activity (r=0.234, P=0.017) especially in the 15 mg lycopene/day group (r=0.485, P=0.003), lymphocyte DNA comet tail moment (r=-0.318, P=0.001), and hs-CRP (r=-0.238, P=0.011). In addition, changes in lycopene correlated with hs-CRP (r=-0.230, P=0.016) and SOD activity (r=0.205, P=0.037).</p> <p>CONCLUSION: An increase in serum lycopene after supplementation can reduce oxidative stress which may play a role in endothelial function</p>	
CVD: BP lipids	Shidfar F	<p>The effects of tomato consumption on serum glucose, apolipoprotein B, apolipoprotein A-I, homocysteine and blood pressure in type 2 diabetic patients.</p> <p>Shidfar F, Froghifar N, Vafa M, Rajab A, Hosseini S, Shidfar S, Gohari M.</p> <p>Int J Food Sci Nutr. 2011 May;62(3):289-94. Epub 2010 Dec 8.</p>	2011	<p>Tomatoes are a rich source of lycopene, β-carotene, potassium, vitamin C, flavonoids, folate and vitamin E that may provide protection against the development of type 2 diabetic patients, so the present study was undertaken to evaluate the effects of tomato intake on serum glucose, homocysteine, apolipoprotein (apo) B, apoA-I and blood pressure in type 2 diabetic patients. In a quasi-experimental study, 32 type 2 diabetes patients received 200 g raw tomato daily for 8 weeks. Serum glucose enzymatically, apoB and apoA-I immunoturbidometrically and homocysteine by high-performance liquid chromatography were measured at the beginning and end of 8 weeks. There were significant decreases in systolic and diastolic blood pressure and also a significant increase in apoA-I at the end of study compared with initial values (P = 0.0001, P = 0.0001 and P = 0.013, respectively). In conclusion, 200 g raw tomato per day had a favored effect on blood pressure and apoA-I so it might be beneficial for reducing cardiovascular risk associated with type 2 diabetes.</p>	Interv
CVD: oxidation lipids inflammation endothelial function	Burton-Freeman B	<p>Protective activity of processed tomato products on postprandial oxidation and inflammation: a clinical trial in healthy weight men and women.</p>	2012	<p>SCOPE: This study was designed to evaluate the ability of tomato rich in lycopene to modify postprandial oxidative stress, inflammation, and endothelial function in healthy weight individuals.</p>	RCT

		<p>Burton-Freeman B, Talbot J, Park E, Krishnankutty S, Edirisinghe I.</p> <p>Mol Nutr Food Res. 2012 Apr;56(4):622-31. doi: 10.1002/mnfr.201100649. Epub 2012 Feb 14.</p>		<p>METHODS AND RESULTS: Twelve women and 13 men (mean age = 27 ± 8 years; mean body mass index= 22 ± 2) consumed high-fat meals known to induce postprandial oxidative stress on two separate occasions containing either processed tomato product or non-tomato alternative. Blood samples were collected at 0, 30, 60, 90, 120 min, then hourly until 360 min. Flow-mediated dilation (FMD) was performed at 0 and 210 min. Endpoints included changes in glucose, insulin, lipids, oxidized low-density lipoprotein (OxLDL), inflammatory cytokines, and FMD. Both meals induced increases in plasma glucose, insulin, and lipid concentrations (p < 0.05). A trend for higher triglycerides at >240 min was observed after the tomato meal (p = 0.006). Tomato significantly attenuated high-fat meal-induced LDL oxidation (p < 0.05) and rise in interleukin-6 (p < 0.0001), a proinflammatory cytokine and inflammation marker.</p> <p>CONCLUSION: The data indicate that consuming tomato products with a meal attenuates postprandial lipemia-induced oxidative stress and associated inflammatory response. The relevance of OxLDL and inflammation to vascular injury suggests a potentially important protective role of tomato in reducing cardiovascular disease risk. ClinicalTrials.gov Registration number - NCT00966550.</p>	
<p>CVD: lipids inflammation BP insulin resistance endothelial function</p>	Thies F	<p>Effect of a tomato-rich diet on markers of cardiovascular disease risk in moderately overweight, disease-free, middle-aged adults: a randomized controlled trial.</p> <p>Thies F, Masson LF, Rudd A, Vaughan N, Tsang C, Brittenden J, Simpson WG, Duthie S, Horgan GW, Duthie G.</p> <p>Am J Clin Nutr. 2012 May;95(5):1013-22. doi: 10.3945/ajcn.111.026286. Epub 2012 Apr 4.</p>	2012	<p>BACKGROUND: Cardiovascular disease (CVD) is a major cause of mortality in the United Kingdom. Epidemiologic studies suggest that consumption of tomato-based foods may lower CVD risk. Such potential benefits have been ascribed in part to high concentrations of lycopene in the tomatoes. However, these findings have not yet been validated by comprehensive intervention trials. OBJECTIVE: The aim of this study was to conduct a single-blind, randomized controlled intervention trial with healthy middle-aged volunteers to assess whether the consumption of tomato-based foods affects recognized biomarkers of CVD risk. DESIGN: After a 4-wk run-in period with a low-tomato diet, 225 volunteers (94 men and 131 women) aged 40-65 y were randomly assigned into 1 of 3 dietary intervention groups and asked to consume a control diet (low in tomato-based foods), a high-tomato-based diet, or a control diet supplemented with lycopene capsules (10 mg/d) for 12 wk. Blood samples were collected at baseline, at 6 wk, and after the intervention and were analyzed for carotenoid and lipid profiles and inflammatory markers. blood pressure, weight, and arterial stiffness were also measured. Dietary intake was also determined during the intervention. RESULTS: None of the systemic markers (inflammatory markers, markers of insulin resistance and sensitivity) changed significantly after the dietary intervention. Moreover, lipid concentrations and arterial stiffness were also unaffected by the interventions. CONCLUSION: These data indicate that a relatively high daily consumption of tomato-based products (equivalent to 32-50 mg lycopene/d) or lycopene supplements (10 mg/d) is ineffective at reducing conventional CVD risk markers in moderately overweight, healthy, middle-aged individuals. This trial was registered at isrctn.org as ISRCTN34203810.</p>	RCT

CVD: oxidation lipids inflammation	Abete I	<p>A regular lycopene enriched tomato sauce consumption influences antioxidant status of healthy young-subjects: A crossover study</p> <p>Abete I, Perez-Cornago A, Navas-Carretero S, Bondia-Pons I, Zulet MA, Martinez, JA</p> <p>Journal of Functional Foods Volume 5, Issue 1, January 2013, Pages 28–35</p>	2013	<p>Tomato and tomato products are known as potential factors to decrease oxidative stress biomarkers. Therefore, the objective was to evaluate the effects of consumption of two tomato sauces with different concentrations of lycopene on oxidative stress markers. Thirty healthy subjects (Men/women: 9/21; Aged 39 ± 6 years old; BMI: 24.5 ± 3.3 kg/m²) were recruited to participate in a double-blind crossover study. Participants had to consume 160 g/day of tomato sauce, while maintaining their usual dietary and physical activity habits. The regular consumption of the high-lycopene tomato sauce induced a significant reduction in the oxidized-LDL cholesterol levels ($-9.27 \pm 16.8\%$; $p < 0.05$). Moreover, total plasma antioxidant capacity tended to increase with the high-lycopene tomato sauce, while it decreased slightly with commercial tomato sauce consumption (2.69 ± 13.4 vs -0.05 ± 0.4; $p = 0.058$). Lipid, glucose profile and C-reactive protein concentrations were stable during both intervention periods, as well as anthropometric and body composition variables. Thus, the daily consumption of 160 g of a high-lycopene tomato sauce improved oxidized-LDL cholesterol levels, evidencing the putative role of lycopene in combination with other bioactive compounds in the prevention of oxidative stress related diseases</p>	RCT
CVD: oxidation lipids inflammation	McEneny J	<p>Lycopene intervention reduces inflammation and improves HDL functionality in moderately overweight middle-aged individuals.</p> <p>McEneny J, Wade L, Young IS, Masson L, Duthie G, McGinty A, McMaster C, Thies F.</p> <p>J Nutr Biochem. 2013 Jan;24(1):163-8. doi: 10.1016/j.jnutbio.2012.03.015. Epub 2012 Jul 21.</p>	2013	<p>The management of overweight subjects by interventions aimed at reducing inflammation is highly desirable. To date, observational studies have identified a link between increased dietary antioxidant intake and reduced cardiovascular morbidity. However, direct trial evidence regarding the ability of antioxidants to influence inflammation is lacking. Therefore, this study examined lycopene's ability to lower systemic and high-density lipoprotein (HDL)-associated inflammation in moderately overweight middle-aged subjects. Serum was collected before and after a 12-week intervention from 54 moderately overweight, middle-aged individuals. Subjects were randomised to one of three groups: control diet (<10 mg lycopene/week), lycopene-rich diet (224-350 mg lycopene/week) and lycopene supplement (70 mg lycopene/week). HDL was subfractionated into HDL(2&3) by rapid ultracentrifugation. Compliance was monitored by assessing lycopene concentration in serum and HDL(2&3). Systemic and HDL-associated inflammation was assessed by measuring serum amyloid A (SAA) levels. HDL functionality was determined by monitoring the activities of paraoxonase-1 (PON-1), cholesteryl ester transfer protein (CETP) and lecithin cholesterol acyltransferase (LCAT). Lycopene increased in serum and HDL(2&3) following both lycopene interventions ($P < .001$, for all), while SAA decreased in serum following the lycopene supplement and in HDL(3) following both lycopene interventions ($P < .05$ for all). PON-1 activity increased in serum and HDL(2&3) in both lycopene groups ($P < .05$, for all). Furthermore, the activity of CETP decreased in serum following the lycopene supplement, while the activity of LCAT increased in serum and HDL(3) following both lycopene interventions ($P < .05$ for all). These results demonstrate that in moderately overweight, middle-aged subjects, increasing lycopene intake leads to changes to HDL(2&3), which we suggest enhanced their antiatherogenic properties. Overall, these results show the heart-protective properties of increased lycopene intake.</p>	RCT

