

## Summary of Research

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Disease: Endpoints of Interest	First Author	Study Title and Complete Citation	Date	Abstract	Study Type
CVD:lipids	Sakamoto H	<p>Elevation of serum carotenoids after continual ingestion of tomato juice.</p> <p>Sakamoto H, Mori H, Ojima F, Ishiguro Y, Arimoto S, Imae Y, Ogawa NT, and Fukuba HJ</p> <p>Jpn Soc Nutr Food Sci, 47 (1994), pp. 93-99.</p>	1994	<p>The concentrations of lycopene and <math>\beta</math>-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 <math>\beta</math>-carotene content of the tomato juice was about one-thirtieth that of lycopene, the <math>\beta</math>-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 <math>\beta</math>-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.</p>	RCT
CVD:lipids	Fuhrman B	<p>Hypocholesterolemic effect of lycopene and beta- carotene is related to suppression of cholesterol synthesis and augmentation of LDL receptor activity in macrophages.</p> <p>Fuhrman B, Elis A, Aviram M.</p>	1997	<p>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-</p>	Interv

		Biochem Biophys Res Commun. 1997 Apr28;233(3):658-62.		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 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	Pool-Zobel BL	Consumption of vegetables reduces genetic damage in humans: first results of a human intervention trial with carotenoid-rich foods.Pool-Zobel BL, Bub A, Müller H, Wollowski I, Rechkemmer G.Carcinogenesis. 1997 Sep;18(9):1847-50.	1997	A human intervention study with vegetable products has been performed in twenty three healthy, non smoking males aged 27-40. It was the aim of the study to assess whether consumption of vegetables containing different carotenoids could protect against DNA damage and oxidative DNA damage. The subjects consumed their normal diets, but abstained from vegetables high in carotenoids throughout the study period. After a 2 week depletion period, they received daily 330 ml tomato juice with 40 mg lycopene (weeks 3 and 4), 330 ml carrot juice with 22.3 mg beta-carotene and 15.7 mg alpha-carotene (weeks 5 and 6), and 10 g dried spinach powder (in water or milk) with 11.3 mg lutein (weeks 7 and 8). Blood was collected weekly and DNA damage was detected in peripheral blood lymphocytes with the 'COMET' assay. Oxidised DNA bases were detected by including an incubation step with endonuclease III. The supplementation of the diet with tomato, carrot or spinach products resulted in a significant decrease in endogenous levels of strand breaks in lymphocyte DNA. Oxidative base damage was significantly reduced during the carrot juice intervention. These findings support the hypothesis that carotenoid containing plant products exert a cancer-protective effect via a decrease in oxidative and other damage to DNA in humans.	Interv
CVD: oxidation lipids	Agarwal S	Tomato lycopene and low density lipoprotein oxidation:a human dietary intervention study. Agarwal S, Rao AV.	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	Interv

		Lipids. 1998 Oct;33(10):981-4.		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.	
CVD: oxidation	Collins AR	Serum carotenoids and oxidative DNA damage in human lymphocytes.  Collins AR, Olmedilla B, Southon S, Granado F, Duthie SJ.  Carcinogenesis. 1998 Dec;19(12):2159-62.	1998	Carotenoids are thought to act as antioxidants in vivo, decreasing oxidative damage to biomolecules and thus protecting against coronary heart disease and cancer. However, human intervention studies with beta-carotene have given equivocal results in terms of cancer incidence. In an alternative molecular epidemiological approach, we have employed the 'comet assay' (single cell alkaline gel electrophoresis) to measure strand breaks, oxidized pyrimidines and altered purines in the DNA of lymphocytes from volunteers supplemented with alpha/beta-carotene, lutein, lycopene or placebo. In addition, we measured concentrations of the main serum carotenoids, and vitamins E and C, by HPLC. We report a significant negative correlation between basal concentrations of total serum carotenoids and oxidized pyrimidines. A similar correlation was seen between individual carotenoids (notably lutein and beta-carotene) and oxidized pyrimidines. However, carotenoid supplementation did not have a significant effect on endogenous oxidative damage. This suggests that there are some factors in the basal diet, probably found in fruit and vegetables, that decrease oxidative damage to DNA. In this case, basal serum carotenoids may simply be markers of consumption of fruit and vegetables, they themselves having little or no protective value.	RCT
CVD: oxidation	Rao AV	Bioavailability and in vivo antioxidant properties of lycopene from tomato products	1998	Oxidative stress is recognized as one of the major contributors of increased risk of cancer. Many recent population studies have established a close link between dietary intake of tomatoes, a major source of the	Interv

		<p>and their possible role in the prevention of cancer.</p> <p>Rao AV, Agarwal S.</p> <p>Nutr Cancer. 1998;31 (3):199-203.</p>		<p>carotenoid antioxidant lycopene, and lowered risk of cancer. A study was conducted on 19 healthy human subjects to evaluate the uptake and in vivo antioxidant properties of ycopene, using a randomized, crossover design. Dietary lycopene was provided by tomato juice, spaghetti sauce, and tomato oleoresin for a period of one week 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 thiobarbituric acid-reactive substances, protein thiols, and 8-oxodeoxyguanosine contents of lymphocyte DNA were assayed to measure lipid, protein, and DNA oxidation. Lycopene was the major carotenoid present in the serum. Dietary supplementation of lycopene resulted in a significant increase in serum lycopene level and diminished amounts of serum thiobarbituric acid-reactive substances. Although not statistically significant, a tendency of lowered protein and DNA oxidation was observed. There was also indication that the lycopene levels increased in a dose-dependent manner in the case of spaghetti sauce and tomato oleoresin. These results indicate that lycopene is readily absorbed from tomato products and may act as an in vivo antioxidant. It may, therefore, play an important role in the prevention of cancer.</p>	
CVD: oxidation	Rao AV	<p>Effect of diet and smoking on serum lycopene and lipid peroxidation.</p> <p>Rao AV, Agarwal S.</p> <p>Nutr Res, 1998;18:713–21.</p>	1998	<p>Lycopene, a naturally present carotenoid in tomatoes and other fruits, has been proposed to have antioxidant and potential anticarcinogenic properties in recent studies. This study was conducted to investigate the effect of diet and smoking on serum lycopene and lipid peroxidation expressed as thiobarbituric acid reactive substances (TBARS) in 20 healthy human subjects. A reduction of 50% in the serum lycopene levels and an increase of 25% in TBARS was observed when subjects were maintained on a lycopene-free diet. Serum lycopene levels were also reduced by 25% following a meal compared to the fasting levels. Serum lycopene levels of habitual smokers were compared with non-smokers. Although the levels were not significantly different between the two groups, serum lycopene levels fell by 40% with a 40% increase in TBARS in smokers following smoking three cigarette. This study showed that the levels of serum lycopene were influenced significantly as a result of oxidative stress in the form of diet induced metabolism and smoking, suggesting <i>in vivo</i> antioxidant properties of lycopene.</p>	Interv
CVD: oxidation	Steinberg FM	<p>Antioxidant vitamin supplementation and lipid peroxidation in smokers.</p>	1998	<p>Previous studies have shown that cigarette smoke enhances lipid peroxidation. This study examined the effect of daily consumption of a tomato-based juice supplemented with vitamin C (600 mg), vitamin E (400</p>	RCT

		<p>Steinberg FM, Chait A.</p> <p>Am J Clin Nutr. 1999 Jun;69(6):1292.</p>		<p>1U, or 400 mg), and beta-carotene (30 mg) on various indexes of lipid peroxidation (breath pentane excretion and susceptibility of LDL to copper-mediated oxidation) in smokers. In addition, plasma lycopene and vitamin concentrations and total peroxy radical trapping potential, a measure of antioxidant defenses, were assessed. Relative to the placebo juice, the vitamin-supplemented juice resulted in a significant decrease in breath-pentane excretion as well as a significant improvement in the resistance of LDL to oxidation. The lag phase of conjugated diene formation lengthened and the propagation rate decreased, indicating a decreased susceptibility of LDL to oxidative modification. Increased concentrations of plasma vitamin C, beta-carotene, and lycopene were found to be significantly correlated with the conjugated diene lag phase and rate of formation. Vitamin E was highly correlated with beta-carotene. Plasma total peroxy radical trapping potential values did not change in response to supplementation. This study thus indicates that an antioxidant-supplemented drink can reduce lipid peroxidation and susceptibility of LDL to oxidation in smokers and may ameliorate the oxidative stress of cigarette smoke.</p>	
CVD:lipids	Böhm V	<p>Intestinal absorption of lycopene from different matrices and interactions to other carotenoids, the lipid status, and the antioxidant capacity of human plasma.</p> <p>Böhm V, Bitsch R.</p> <p>Eur J Nutr. 1999 Jun;38(3):118-25.</p>	1999	<p>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.</p> <p>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.</p> <p>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 supplementation started, and then</p>	RCT

				<p>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 <math>\mu\text{mol/l}</math>) 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 <math>0.33 \pm 0.05 \text{ mmol/l}</math> and TRAP values to <math>1.0 \pm 0.1 \text{ mmol/l}</math> 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	Dugas TR	Dietary supplementation with beta-carotene, but not with lycopene, inhibits endothelial cell-mediated oxidation of low-density lipoprotein. Dugas TR, Morel DW, Harrison EH. Free Radic Biol Med. 1999 May;26(9-10):1238-44	1999	Carotenoids may protect low-density lipoprotein from oxidation, a process implicated in the development of atherosclerosis. Our previous studies showed that in vitro enrichment of low-density lipoprotein (LDL) with beta-carotene protected it from cell-mediated oxidation. However, in vitro enrichment with either lutein or lycopene actually enhanced oxidation of the LDL. In the present studies we have examined the impact of LDL carotenoid content on its oxidation by human aortic endothelial cells	Interv

				(EaHy-1) in culture, comparing the effects of in vivo supplementation with in vitro enrichments. The beta-carotene content in human LDL was increased three- to sixfold by daily supplementation with 15 mg beta-carotene for 4 weeks, and the lycopene content of LDL in other individuals was increased two- to threefold by ingestion of one glass (12 ounce) of tomato juice daily for 3 weeks. LDL isolated from these healthy, normolipidemic donors not taking supplemental carotenoid was incubated at 0.25 mg protein/ml with EaHy-1 cells in Ham's F-10 medium for up to 48 h. Following dietary beta-carotene supplementation, LDL oxidation (as assessed by formation of lipid hydroperoxides) was markedly inhibited, to an even greater extent than was observed for LDL enriched in vitro with beta-carotene (that resulted in an 11- to 12-fold increase in LDL beta-carotene). No effect on cell-mediated oxidation was observed, however, for LDL enriched in vivo with lycopene. Thus, beta-carotene appears to function as an antioxidant in protecting LDL from cell-mediated oxidation although lycopene does not. The fact that the three- to sixfold enrichments of LDL with beta-carotene achieved by dietary supplementation were more effective in inhibiting oxidation than the 11- to 12-fold enrichments achieved by an in vitro method suggests that dietary supplementation is a more appropriate procedure for studies involving the enrichment of lipoprotein with carotenoids.	
CVD: oxidation	Rehman A	Tomato consumption modulates oxidative DNA damage in humans.  Rehman A, Bourne LC, Halliwell B, Rice-Evans CA.  Biochem Biophys Res Commun. 1999 Sep 7;262(3):828-31.	1999	Consumption of a single serving of tomatoes by healthy human volunteers was sufficient to alter levels of oxidative DNA base damage in white cell DNA within 24 h. Levels of the mutagenic oxidized purine base 8-hydroxyguanine decreased, especially in those subjects whose initial levels of this base were higher than the mean. However, total DNA base damage remained unchanged since levels of 8-hydroxyadenine rose. The ability of tomato consumption to modulate oxidative DNA damage in the short term may indicate why daily consumption of fruits and vegetables is beneficial in decreasing cancer incidence.	Interv
CVD: oxidation	Riso P	Does tomato consumption effectively increase the resistance of lymphocyte DNA to oxidative damage?  Riso P, Pinder A, Santangelo A, Porrini M.	1999	BACKGROUND: Lycopene, the main carotenoid in tomato, has been shown to be a potent antioxidant in vitro. However, there is no significant evidence of its antioxidant action in vivo.  OBJECTIVE: We evaluated the effect of tomato intake on plasma carotenoid concentrations and lymphocyte resistance to oxidative stress.  DESIGN: Ten healthy women (divided into 2 groups of 5 subjects each) ate	RCT

		Am J Clin Nutr.1999 Apr;69(4):712-8.		<p>a diet containing tomato puree (providing 16.5 mg lycopene) and a tomato-free diet for 21 d each in a crossover design. Before and after each diet period, plasma carotenoid concentrations and primary lymphocyte resistance to oxidative stress (evaluated by means of single-cell gel electrophoresis) were analyzed.</p> <p>RESULTS: After the first 21-d experimental period, total plasma lycopene concentrations increased by 0.5 micromol/L(95% CI: 0.14, 0.87) in the group that consumed the tomato diet and decreased by 0.2 micromol/L (95% CI: -0.11, -0.30) in the group that consumed the tomato-free diet (P &lt; 0.001). Tomato consumption also had an effect on cellular antioxidant capacity: lymphocyte DNA damage after ex vivo treatment with hydrogen peroxide decreased by 33% (95% CI: 0.8% , 61% ; P &lt; 0.05) and by 42% (95% CI: 5.1% , 78% ; P &lt; 0.05) in the 2 groups of subjects after consumption of the tomato diet.</p> <p>CONCLUSION: The consumption of tomato products may reduce the susceptibility of lymphocyte DNA to oxidative damage</p>	
CVD: oxidation	Sutherland WH	<p>Supplementation with tomato juice increases plasma lycopene but does not alter susceptibility to oxidation of low-density lipoproteins from renal transplant recipients.</p> <p>Sutherland WH, Walker RJ, De Jong SA, Upritchard JE.</p> <p>Clin Nephrol.1999 Jul;52(1):30-6</p>	1999	<p>AIM: Oxidative stress and susceptibility of low-density lipoproteins (LDL) to oxidation are increased in renal transplant recipients. The aim of this study was to determine the effect of dietary supplementation with tomato juice on plasma levels of the antioxidant lycopene, serum indices of lipid peroxidation (fluorescent lipid oxidation products (FLOP) and thiobarbituric acid-reacting substances (TBARS)) and the resistance of isolated low-density lipoprotein (LDL) to oxidation (lag time) in patients with a kidney graft.SUBJECTS AND</p> <p>METHODS: Fifteen patients were randomized to daily consumption of either tomato juice or synthetic orange drink for 4 weeks in a crossover study. Plasma lycopene levels were significantly higher (1.57 micromol/l versus 0.91 micromol/l, p = 0.015) while serum FLOP and TBARS and resistance of LDL to oxidation were not significantly different during supplementation with tomato juice compared with orange drink. At baseline, serum levels of lycopene and FLOP were abnormally high and serum FLOP was correlated significantly with plasma cyclosporine levels (r = 0.646, p = 0.016).</p> <p>CONCLUSION: In conclusion, these data suggest that increased oxidative stress and susceptibility of LDL to oxidation may not be reduced by</p>	Interv



				increasing plasma lycopene levels with regular consumption of tomato juice in renal transplant recipients.	
CVD: oxidation	Bub A	<p>Moderate intervention with carotenoid-rich vegetable products reduces lipid peroxidation in men.</p> <p>Bub A, Watzl B, Abrahamse L, Delinsee H, Adam S, Wever J, Muller H, Rechkemmer G.</p> <p>J Nutr. 2000 Sep;130(9):2200-6.</p>	2000	<p>Because of their antioxidant properties, carotenoids may have beneficial effects in preventing cancer and cardiovascular disease. However, in humans consuming carotenoid-rich vegetables, data concerning the antioxidant effects of carotenoids are rather scarce. A human intervention trial was conducted, therefore, to determine whether a moderately increased consumption of carotenoid-rich vegetables would influence the antioxidant status in 23 healthy men. This short-term feeding study lasted 8 wk during which the men consumed a low carotenoid diet. A 2-wk low carotenoid period was followed by daily consumption of 330 mL tomato juice, then by 330 mL carrot juice and then by 10 g of spinach powder, each for 2 wk. Antioxidant status [water-soluble antioxidants in serum, ferric reducing ability of plasma (FRAP) and antioxidant enzyme activities] and lipid peroxidation (plasma malondialdehyde and ex vivo oxidation of LDL) were determined. In a subgroup of 10 men, lipoprotein carotenoids were measured. The consumption of carotenoid-rich vegetables significantly increased selected carotenoids in lipoproteins but had only minor effects on their relative distribution pattern. Tomato juice consumption reduced plasma thiobarbituric acid reactive substances (TBARS) by 12% (P: &lt; 0.05) and lipoprotein oxidizability in terms of an increased lag time (18%, P: &lt; 0.05). Carrot juice and spinach powder had no effect on lipid peroxidation. Water-soluble antioxidants, FRAP, glutathione peroxidase and reductase activities did not change during any study period. In evaluating the low carotenoid diet, we conclude that the additional consumption of carotenoid-rich vegetable products enhanced lipoprotein carotenoid concentrations, but only tomato juice reduced LDL oxidation in healthy men.</p>	Interv
CVD: oxidation	Carroll YL	<p>Lipoprotein carotenoid profiles and the susceptibility of low density lipoprotein to oxidative modification in healthy elderly volunteers.</p> <p>Carroll YL, Corridan BM, Morrissey PA.</p> <p>Eur J Clin Nutr. 2000 Jun;54(6):500-7.</p>	2000	<p>OBJECTIVES: To determine antioxidant levels in plasma, low density lipoprotein (LDL) and high density lipoprotein (HDL) before and after supplementation with a carotene mixture or lycopene; to examine the interrelationships between carotenoids and tocopherols in plasma, LDL and HDL under normal dietary conditions and after supplementation with carotene or lycopene; and to investigate whether supplementation with a carotene mixture or lycopene could enhance the ability of LDL to withstand oxidative stress in vitro, in a group of healthy elderly people</p>	RCT

				<p>aged &gt; or =65 y.</p> <p>DESIGN: Randomized placebo controlled double blind study.SETTING: Free living urban adults in Ireland. Subjects: Fifty-one volunteers aged &gt; or =65 y.INTERVENTIONS: Volunteers were each provided with capsules providing either 13.3 mg lycopene, or 11.9 mg carotene or placebo for 12 weeks.</p> <p>RESULTS: Both absolute and cholesterol standardized plasma carotenoid concentrations correlated strongly with LDL and HDL concentrations of carotenoids before and after supplementation with carotene or lycopene. Supplementation with a carotene mixture or lycopene had no effect on oxidative modification of LDL in vitro despite significant increases in plasma and LDL concentrations of lycopene, alpha-carotene and beta-carotene.</p> <p>CONCLUSIONS: The results of this study suggest that, in unsupplemented individuals, plasma can act as a biomarker of carotenoid and gamma-tocopherol concentrations in both LDL and HDL. Supplementation with carotenes or lycopene do not reduce or delay oxidation of LDL. These results support the assumption that carotenoids, such as beta-carotene and lycopene, may show protective effects because they are good markers of fruit and vegetable intake.</p>	
CVD: oxidation	Chopra M	<p>Influence of increased fruit and vegetable intake on plasma and lipoprotein carotenoids and LDL oxidation in smokers and nonsmokers.</p> <p>Chopra M, O'Neill ME, Keogh N, Wortley G, Southon S, Thurnham DI.</p> <p>Clin Chem.2000 Nov;46(11):1818-29.</p>	2000	<p>BACKGROUND: Epidemiological studies suggest a cardioprotective role for carotenoid-rich foods. Smokers have a high risk of cardiovascular disease and low dietary intake and plasma concentrations of carotenoids. The aim of this study was to determine the carotenoid response of smokers and nonsmokers to increased intake of 300-400 g of vegetables and its effect on LDL oxidation.</p> <p>METHODS: After a depletion period of 8 days, 34 healthy females (18 nonsmokers, 16 smokers) were supplemented with beta-carotene- and lutein-rich (green) and lycopene-rich (red) vegetable foods, each for 7 days.</p> <p>RESULTS: Baseline concentrations (mean +/- SD) of plasma beta-carotene (0.203+/-0.28 micromol/L vs. 0.412+/-0.34 micromol/L; P &lt;0.005) and lutein (0.180 +/-0.10 vs. 0.242+/-0.11 micromol/L; P&lt;0.05) but not lycopene (0.296+/-0.10 vs.0.319+/-0.33 micromol/L) were significantly lower in smokers compared with nonsmokers. After supplementation, the change (supplementation minus depletion) in plasma beta-carotene (0.152+/-</p>	Interv

				<p>0.43 vs. 0.363+/-0.29 micromol/L in smokers vs. nonsmokers; P = 0.002) and LDL lutein (0.015+/-0.03 vs. 0.029+/-0.03 micromol/mmol cholesterol; P = 0.01) was significantly lower in smokers than nonsmokers. Green-vegetable supplementation had no effect on the resistance of LDL to oxidation (lag-phase) in either group. After red-vegetable supplementation, plasma and LDL lycopene concentrations were increased in both groups, but only nonsmokers showed a significant increase in the lag-phase (44.9+/-9.5 min at baseline, 41.4+/-6.5 min after depletion, and 49.0+/-8.9 min after supplementation; P&lt;0.01) compared with depletion.</p> <p>CONCLUSIONS: In this short-term intervention study, a dietary intake of &gt;40 mg/day of lycopene by a group of nonsmoking individuals significantly reduced the susceptibility of LDL to oxidation, whereas an equivalent increase in lycopene by a group of smokers showed no such effect.</p>	
CVD: oxidation	Fuhrman B	<p>Lycopene synergistically inhibits LDL oxidation in combination with vitamin E, glabridin, rosmarinic acid, carnosic acid, or garlic.</p> <p>Fuhrman B, Volkova N, Rosenblatt M, Aviram M.</p> <p>Antioxid Redox Signal. 2000 Fall;2(3):491-506.</p>	2000	<p>Several lines of evidence suggest that oxidatively modified low-density lipoprotein (LDL) is atherogenic, and that atherosclerosis can be attenuated by natural antioxidants, which inhibit LDL oxidation. This study was conducted to determine the effect of tomato lycopene alone, or in combination with other natural antioxidants, on LDL oxidation. LDL (100 microg of protein/ml) was incubated with increasing concentrations of lycopene or of tomato oleoresin (lipid extract of tomatoes containing 6% lycopene, 0.1% beta-carotene, 1% vitamin E, and polyphenols), after which it was oxidized by the addition of 5 micromol/liter of CuSO4. Tomato oleoresin exhibited superior capacity to inhibit LDL oxidation in comparison to pure lycopene, by up to five-fold [97% vs. 22% inhibition of thiobarbituric acid reactive substances (TBARS) formation, and 93% vs. 27% inhibition of lipid peroxides formation, respectively]. Because tomato oleoresin also contains, in addition to lycopene, vitamin E, flavonoids, and phenolics, a possible cooperative interaction between lycopene and such natural antioxidants was studied. A combination of lycopene (5 micromol/liter) with vitamin E (alpha-tocopherol) in the concentration range of 1-10 micromol/liter resulted in an inhibition of copper ion-induced LDL oxidation that was significantly greater than the expected additive individual inhibitions. The synergistic antioxidative effect of lycopene with vitamin E was not shared by gamma-tocotrienol. The polyphenols glabridin (derived from licorice), rosmarinic acid or carnosic acid (derived from rosemary), as well as garlic (which contains a mixture of natural antioxidants) inhibited LDL oxidation in a dose-dependent manner. When lycopene (5 micromol/liter) was added to LDL in</p>	Interv

				<p>combination with glabridin, rosmarinic acid, carnosic acid, or garlic, synergistic antioxidative effects were obtained against LDL oxidation induced either by copper ions or by the radical generator AAPH. Similar interactive effects seen with lycopene were also observed with beta-carotene, but, however, to a lesser extent of synergism. Because natural antioxidants exist in nature in combination, the in vivo relevance of lycopene in combination with other natural antioxidants was studied. Four healthy subjects were administered a fatty meal containing 30 mg of lycopene in the form of tomato oleoresin. The lycopene concentration in postprandial plasma was elevated by 70% in comparison to plasma obtained before meal consumption. Postprandial LDL isolated 5 hr after meal consumption exhibited a significant (<math>p &lt; 0.01</math>) reduced susceptibility to oxidation by 21% . We conclude that lycopene acts synergistically, as an effective antioxidant against LDL oxidation, with several natural antioxidants such as vitamin E, the flavonoid glabridin, the phenolics rosmarinic acid and carnosic acid, and garlic. These observations suggest a superior antiatherogenic characteristic to a combination of different natural antioxidants over that of an individual one.</p>	
CVD: oxidation	Porrini M	<p>Lymphocyte lycopene concentration and DNA protection from oxidative damage is increased in women after a short period of tomato consumption.</p> <p>Porrini M, Riso P.</p> <p>J Nutr. 2000 Feb;130(2):189-92.</p>	2000	<p>Several epidemiologic studies have suggested a role of tomato products in protecting against cancer and chronic diseases. In nine adult women, we evaluated whether the consumption of 25 g tomato puree (containing 7 mg lycopene and 0.3 mg beta-carotene) for 14 consecutive days increased plasma and lymphocyte carotenoid concentration and whether this was related to an improvement in lymphocyte resistance to an oxidative stress (500 micromol/L hydrogen peroxide for 5 min). Before and after the period of tomato intake, carotenoid concentrations were analyzed by HPLC and lymphocyte resistance to oxidative stress by the Comet assay, which detects DNA strand breaks. Intake of tomato puree increased plasma (<math>P &lt; 0.001</math>) and lymphocyte (<math>P &lt; 0.005</math>) lycopene concentration and reduced lymphocyte DNA damage by approximately 50% (<math>P &lt; 0.0001</math>). Beta-carotene concentration increased in plasma (<math>P &lt; 0.05</math>) but not in lymphocytes after tomato puree consumption. An inverse relationship was found between plasma lycopene concentration (<math>r = -0.82</math>, <math>P &lt; 0.0001</math>) and lymphocyte lycopene concentration (<math>r = -0.62</math>, <math>P &lt; 0.01</math>) and the oxidative DNA damage. In conclusion, small amounts of tomato puree added to the diet over a short period can increase carotenoid concentrations and the resistance of lymphocytes to oxidative stress.</p>	Interv

CVD: oxidation inflammation endothelial function markers	Upritchard JE	<p>Effect of supplementation with tomato juice, vitamin E, and vitamin C on LDL oxidation and products of inflammatory activity in type 2 diabetes.</p> <p>Upritchard JE, Sutherland WH, Mann JI.</p> <p>Diabetes Care.2000 Jun;23(6):733-8.</p>	2000	<p>OBJECTIVE: To compare the effects of short-term dietary supplementation with tomato juice, vitamin E, and vitamin C on susceptibility of LDL to oxidation and circulating levels of C-reactive protein (C-RP) and cell adhesion molecules in patients with type 2 diabetes. RESEARCH DESIGN AND</p> <p>METHODS: There were 57 patients with well-controlled type 2 diabetes aged &lt;75 years treated with placebo for 4 weeks and then randomized to receive tomato juice (500 ml/day), vitamin E (800 U/day), vitamin C (500 mg/day), or continued placebo treatment for 4 weeks. Susceptibility of LDL to oxidation (lag time) and plasma concentrations of lycopene, vitamin E, vitamin C, C-RP, vascular cell adhesion molecule 1, and intercellular adhesion molecule 1 were measured at the beginning of the study, after the placebo phase, and at the end of the study.</p> <p>RESULTS: Plasma lycopene levels increased nearly 3-fold (P = 0.001), and the lag time in isolated LDL oxidation by copper ions increased by 42% (P = 0.001) in patients during supplementation with tomato juice. The magnitude of this increase in lag time was comparable with the corresponding increase during supplementation with vitamin E (54%). Plasma C-RP levels decreased significantly (-49%, P = 0.004) in patients who received vitamin E. Circulating levels of cell adhesion molecules and plasma glucose did not change significantly during the study.</p> <p>CONCLUSIONS: This study indicates that consumption of commercial tomato juice increases plasma lycopene levels and the intrinsic resistance of LDL to oxidation almost as effectively as supplementation with a high dose of vitamin E, which also decreases plasma levels of C-RP, a risk factor for myocardial infarction, in patients with diabetes. These findings may be relevant to strategies aimed at reducing risk of myocardial infarction in patients with diabetes.</p>	RCT
CVD: oxidation	Hininger IA	<p>No significant effects of lutein, lycopene or beta-carotene supplementation on biological markers of oxidative stress and LDL oxidizability in healthy adult subjects.</p> <p>Hininger IA, Meyer-Wenger A, Moser U, Wright A, Southon S,</p>	2001	<p>OBJECTIVE: The objective of this study was to determine the effect of individual carotenoid supplementation on biochemical indices of oxidative status in apparently healthy adult males.</p> <p>METHODS: The study was a placebo controlled single blind study. Healthy male volunteers (n= 175) were assigned to four groups. They received daily supplements of beta-carotene (15 mg), lutein (15 mg), lycopene (15</p>	RCT

		<p>Thurnham D, Chopra M, Van Den Berg H, Olmedilla B, Favier AE, Roussel AM.</p> <p>J Am Coll Nutr. 2001 Jun;20(3):232-8.</p>		<p>mg) and placebo for three months. The effects of the supplementation on antioxidant status were monitored by plasma carotenoid, vitamin C and A levels, glutathione (GSH and GSSG) concentrations, protein SH groups, erythrocyte antioxidant enzyme activities (Cu-Zn SOD, Se-GSH-Px) and susceptibility of LDL to copper-induced oxidation.</p> <p>RESULTS: beta-carotene, lycopene and lutein supplementation led to significant plasma and LDL increases in each of these carotenoids, without modifications of other carotenoid levels in plasma or in LDL. The supplementation failed to enhance the resistance of LDL to oxidation or to modify the LDL polyunsaturated/ saturated fatty acid ratio. Vitamin C, GSH, protein SH groups and antioxidant metalloenzyme activities were also unchanged.</p> <p>CONCLUSION: We did not observe beneficial or adverse effects of lutein, lycopene or beta-carotene supplementation on biomarkers of oxidative stress. In apparently healthy subjects, carotenoid supplementation does not lead to significantly measurable improvement in antioxidant defenses.</p>	
CVD: oxidation	Maruyama C	<p>Effects of tomato juice consumption on plasma and lipoprotein carotenoid concentrations and the susceptibility of low density lipoprotein to oxidative modification.</p> <p>Maruyama C, Imamura K, Oshima S, Suzukawa M, Egami S, Tonomoto M, Baba N, Harada M, Ayaori M, Inakuma T, Ishikawa T.</p> <p>J Nutr Sci Vitaminol (Tokyo). 2001 Jun;47(3):213-21</p>	2001	<p>Effects of tomato juice supplementation on the carotenoid concentration in lipoprotein fractions and the oxidative susceptibility of LDL were investigated in 31 healthy Japanese female students. These subjects were randomized to one of three treatment groups; Control, Low and High. The Control, Low and High groups consumed 480 g of a control drink, 160 g of tomato juice plus 320 g of the control drink, and 480 g of tomato juice, providing 0, 15 and 45 mg of lycopene, respectively, for one menstrual cycle. The ingestion of tomato juice, rich in lycopene but having little beta-carotene, increased both lycopene and beta-carotene. Sixty-nine percent of lycopene in plasma was distributed in the LDL fraction and 24% in the HDL fraction. In the Low group, the lycopene concentration increased 160% each in the VLDL+IDL, LDL and HDL fractions (<math>p &lt; 0.01</math>). In the High group, the lycopene concentration increased 270% each in the VLDL+IDL and LDL fractions, and 330% in the HDL fraction (<math>p &lt; 0.01</math>). Beta-carotene also increased 120% and 180% in LDL fractions of the Low and the High groups, respectively. Despite these carotenoid increases in LDL, the lag time before oxidation was not prolonged as compared with that of the Control group. The propagation rate decreased significantly after consumption in the High group. Multiple regression analysis showed a positive correlation between lag time changes and changes in the alpha-tocopherol concentration per triglyceride in LDL, and a negative correlation between propagation rate changes and changes in the</p>	RCT

				<p>lycopene concentration per phospholipid in LDL. These data suggest that alpha-tocopherol is a major determinant in protecting LDL from oxidation, while lycopene from tomato juice supplementation may contribute to protect phospholipid in LDL, from oxidation. Thus, oral intake of lycopene might be beneficial for ameliorating atherosclerosis.</p>	
CVD: oxidation BP	John JH	<p>Effects of fruit and vegetable consumption on plasma antioxidant concentrations and blood pressure: a randomised controlled trial.</p> <p>John JH, Ziebland S, Yudkin P, Roe LS, Neil HA; Oxford Fruit and Vegetable Study Group.</p> <p>Lancet. 2002 Jun 8;359(9322):1969-74.</p>	2002	<p>BACKGROUND: High dietary intakes of fruit and vegetables are associated with reduced risks of cancer and cardiovascular disease. Short-term intensive dietary interventions in selected populations increase fruit and vegetable intake, raise plasma antioxidant concentrations, and lower blood pressure, but long-term effects of interventions in the general population are not certain. We assessed the effect of an intervention to increase fruit and vegetable consumption on plasma concentrations of antioxidant vitamins, daily fruit and vegetable intake, and blood pressure.</p> <p>METHODS: We undertook a 6-month, randomised, controlled trial of a brief negotiation method to encourage an increase in consumption of fruit and vegetables to at least five daily portions. We included 690 healthy participants aged 25-64 years recruited from a primary-care health centre.</p> <p>FINDINGS: Plasma concentrations of alpha-carotene, beta-carotene, lutein, beta-cryptoxanthin, and ascorbic acid increased by more in the intervention group than in controls (significance of between-group differences ranged from p=0.032 to 0.0002). Groups did not differ for changes in lycopene, retinol, alpha-tocopherol, gamma-tocopherol, or total cholesterol concentrations. Self-reported fruit and vegetable intake increased by a mean 1.4 (SD 1.7) portions in the intervention group and by 0.1 (1.3) portion in the control group (between-group difference=1.4, 95% CI 1.2-1.6; p&lt;0.0001). Systolic blood pressure fell more in the intervention group than in controls (difference=4.0 mm Hg, 2.0-6.0; p&lt;0.0001), as did diastolic blood pressure (1.5 mm Hg, 0.2-2.7; p=0.02).</p> <p>INTERPRETATION: The effects of the intervention on fruit and vegetable consumption, plasma antioxidants, and blood pressure would be expected to reduce cardiovascular disease in the general population. Comment in: Lancet. 2002 Nov 30;360(9347):1785-6; author reply 1786. Lancet. 2002 Nov 30;360(9347):1786.</p>	RCT

CVD: oxidation	Olmedilla B	<p>A European multicentre, placebo-controlled supplementation study with alpha-tocopherol, carotene-rich palm oil, lutein or lycopene: analysis of serum responses.</p> <p>Olmedilla B, Granado F, Southon S, Wright AJ, Blanco I, Gil-Martinez E, van den Berg H, Thurnham D, Corridan B, Chopra M, Hinnerling I.</p> <p>Clin Sci (Lond). 2002 Apr;102(4):447-56.</p>	2002	<p>Increased levels of oxidative stress have been implicated in tissue damage and the development of chronic diseases, and dietary antioxidants may reduce the risk of oxidative tissue damage. As part of a European multicentre project, several studies were undertaken with the aim of testing whether the consumption of foods rich in carotenoids reduces oxidative damage to human tissue components. We describe here the serum response of carotenoids and tocopherols upon supplementation with carotenoids from natural extracts (alpha-carotene+beta-carotene, lutein or lycopene; 15 mg/day) and/or with alpha-tocopherol (100 mg/day) in a multicentre, placebo-controlled intervention study in 400 healthy male and female volunteers, aged 25-45 yrs, from five European regions (France, Northern Ireland, Republic of Ireland, The Netherlands and Spain). Supplementation with alpha-tocopherol increased serum alpha-tocopherol levels, while producing a marked decrease in serum gamma-tocopherol. Supplementation with alpha- + beta-carotene (carotene-rich palm oil) resulted in 14-fold and 5-fold increases respectively in serum levels of these carotenoids. Supplementation with lutein (from marigold extracts) elevated serum lutein (approx. 5-fold), zeaxanthin (approx. doubled) and ketocarotenoids (although these were not present in the supplement), whereas lycopene supplementation (from tomato paste) resulted in a 2-fold increase in serum lycopene. The isomer distributions of beta-carotene and lycopene in serum remained constant regardless of the isomer composition in the capsules. In Spanish volunteers, additional data showed that the serum response to carotenoid supplementation reached a plateau after 4 weeks, and no significant side effects (except carotenodermia) or changes in biochemical or haematological indices were observed throughout the study. This part of the study describes dose-time responses, isomer distribution, subject variability and side effects during supplementation with the major dietary carotenoids in healthy subjects. Also, oxidative stress assessment revealing no remarkable findings.</p>	RCT
CVD: oxidation	Porrini M	<p>Spinach and tomato consumption increases lymphocyte DNA resistance to oxidative stress but this is not related to cell carotenoid concentrations.</p> <p>Porrini M, Riso P, Oriani G.</p> <p>Eur J Nutr. 2002 Jun;41 (3):95-100.</p>	2002	<p>BACKGROUND: The increased consumption of fruit and vegetables has been linked to protection against different chronic diseases, but the dietary constituents responsible for this association have not been clearly identified.</p> <p>AIM OF THE STUDY: We evaluated the effect of spinach and spinach+tomato puree consumption on cell DNA resistance to an oxidative stress.</p>	Interv



				<p><b>METHODS:</b> To this aim, in a dietary controlled intervention study, 9 healthy female volunteers consumed a basal diet low in carotenoids (&lt; 600 microg/day) enriched with daily portions (150 g) of spinach (providing about 9 mg lutein, 0.6 mg zeaxanthin, 4 mg beta-carotene) for 3 weeks (from day 0 to day 21) followed by a 2 week wash-out period (basal diet) and finally another 3 weeks (from day 35 to day 56) of diet enriched with daily portions of spinach (150 g) + tomato puree (25 g, providing about 7 mg lycopene, 0.3 mg beta-carotene). At the beginning and the end of each period of vegetable intake, blood samples were collected for lymphocyte separation. Carotenoid concentrations of lymphocytes were determined by HPLC and DNA damage was evaluated by the comet assay following an ex vivo treatment with H<sub>2</sub>O<sub>2</sub>.</p> <p><b>RESULTS:</b> During the first period of spinach consumption, lymphocyte lutein concentration did not increase significantly (1.6 to 2.2 mmol/10<sup>12</sup> cells) while lycopene and beta-carotene concentrations decreased significantly (1.0 to 0.1 mmol/10<sup>12</sup> cells, P &lt; 0.001, and 2.2 to 1.2 mmol/10<sup>12</sup> cells, P &lt; 0.05, respectively). Lutein and lycopene concentrations increased after spinach+tomato puree consumption (1.2 to 3.5 mmol/10<sup>12</sup> cells, P &lt; 0.01, and 0.1 to 0.7 mmol/10<sup>12</sup> cells, P &lt; 0.05, respectively). The increase may be attributed to the addition of tomato puree to spinach; however, the different concentrations of carotenoids in lymphocytes registered at the beginning of the two intervention periods may have affected the results. DNA resistance to H<sub>2</sub>O<sub>2</sub> insult increased significantly after both the enriched diets (P &lt; 0.01); however, no "additive effect" was seen after spinach + tomato puree consumption. In the spinach + tomato intervention period an inverse correlation was observed between lymphocyte lycopene concentration and DNA damage, but this seems not able to explain the protection observed.</p> <p><b>CONCLUSIONS:</b> The consumption of carotenoid-rich foods even for a short period of time gives protection against oxidative stress. The results obtained seem to suggest that this protective role is not specifically related to carotenoids. However they may contribute together with other substances present in vegetables to lymphocyte resistance to oxidative damage.</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	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	Interv

		humans. Ahuja KD, Ashton EL, Ball MJ.  Clin Sci (Lond). 2003 Sep;105(3):355-61.		(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 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.	
CVD: oxidation	Hadley CW	The consumption of processed tomato products enhances plasma lycopene concentrations in association with a reduced lipoprotein sensitivity to oxidative damage.  Hadley CW, Clinton SK, Schwartz SJ.  J Nutr. 2003Mar;133(3):727-32	2003	Lycopene, the predominant carotenoid in tomatoes, is hypothesized to mediate the health benefits of tomato products. We designed a study to examine the change in plasma lycopene and resistance of lipoproteins to ex vivo oxidative stress. Healthy individuals (n = 60; age >40 y; 30 men/30 women) consumed a lycopene-free diet for 1 wk and were subsequently randomized to receive 35 +/- 1, 23 +/- 1 or 25 +/- 1 mg lycopene/d from Campbell's Condensed Tomato Soup (CS), Campbell's Ready To Serve Tomato Soup (RTS) or V8 Vegetable Juice (V8), respectively, for 15 d. Total plasma lycopene concentrations decreased from 0.499 +/- 0.044 to 0.322 +/- 0.027 (35%, P < 0.0001) micro mol/L for the 60 participants during the 7-d washout period. After intervention, total lycopene concentrations increased for those consuming CS, RTS and V8 (compared with the washout period for each group) to 0.784 +/- 0.083 (123%, P < 0.0001), 0.545 +/- 0.061 (57%, P < 0.01) and 0.569 +/- 0.061 (112%, P < 0.0001) micro mol/L, respectively. The concentrations of all lycopene isomers decreased during the washout period. As a percentage of plasma total lycopene isomers for the 60 subjects, all-trans-lycopene decreased from 44.4 +/- 1.2 to 39.6 +/- 1.2 (P < 0.0001), whereas total cis-lycopene isomers increased from 55.6 +/- 1.2 to 60.4 +/- 1.2 (P < 0.0001) during the washout period, a shift that was reversed by consumption of tomato products for 15 d. The ex vivo lipoprotein oxidation lag period, used as a measure of antioxidant capacity, increased significantly from 64.7 +/- 2.4 min at the end of the washout period (all groups) to 70.1 +/- 4.0 (P < 0.05), 68.3 +/- 2.4 (P < 0.05)	Interv

				and 71.7 +/- 4.0 min (P < 0.01) after treatment for the CS, RTS and V8 groups, respectively. This study shows that lycopene concentrations and isomer patterns change rapidly with variation in dietary intake. In addition, 15 d of tomato product consumption significantly enhanced the protection of lipoproteins to ex vivo oxidative stress.	
CVD: oxidation lipids	Kiokias S	Dietary supplementation with a natural carotenoid mixture decreases oxidative stress.  Kiokias S, Gordon MH.  Eur J Clin Nutr. 2003 Sep;57(9):1135-40.	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.SETTING: Hugh Sinclair Unit of Human Nutrition, School of Food Biosciences, The University of Reading, WhiteknightsPO Box 226, Reading RG6 6AP, UK.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	Visioli F	Protective activity of tomato products on in vivo markers of lipid oxidation.	2003	BACKGROUND: It has been suggested that regular consumption of tomato products improves antioxidant defenses due to their endogenous antioxidant compounds, notably lycopene.	Interv

		<p>Visioli F, Riso P, Grande S, Galli C, Porrini M.</p> <p>Eur J Nutr. 2003Aug;42(4):201-6.</p>		<p>AIM OF THE STUDY: We evaluated the effects of tomato consumption on parameters of lipid oxidation in healthy human volunteers.</p> <p>METHODS: Twelve females (enrolled at T-7), after a one-week of carotenoid-poor diet (T0), were instructed to supplement the same diet with different tomato products (raw, sauce, and paste), thereby providing approximately eight mg lycopene/day for three weeks (T21). Blood samples were periodically collected in order to evaluate plasma carotenoid concentrations, plasma antioxidant capacity, and susceptibility of LDL to metal ion-induced oxidation. Furthermore, 8-iso-PGF(2alpha), a marker of in vivo oxidative stress, was analyzed in the 24-hour urine.</p> <p>RESULTS: Carotenoid concentrations decreased significantly during the carotenoid-poor diet (<math>P &lt; 0.05</math>), while lycopene concentrations increased significantly after tomato consumption (<math>P &lt; 0.001</math>). The antioxidant capacity of plasma did not vary during the study. Conversely, LDL oxidizability decreased after tomato consumption, as demonstrated by a shortening of the lag phase (<math>P &lt; 0.001</math>). This parameter was significantly correlated with lycopene concentration (<math>r = 0.36</math>, <math>P &lt; 0.05</math>). The excretion of 8-iso-PGF(2alpha) in urine was also significantly lower (-53%, <math>P &lt; 0.05</math> compared with T0) after tomato supplementation.</p> <p>CONCLUSIONS: These results further support a role for tomato products in the prevention of lipid peroxidation, a risk factor of atherosclerosis and cardiovascular disease.</p>	
CVD:inflammation	Watzl B	<p>Supplementation of a low-carotenoid diet with tomato or carrot juice modulates immune functions in healthymen.</p> <p>Watzl B, Bub A, Briviba K, Reckemmer G.</p> <p>Ann Nutr Metab. 2003;47(6):255-61.</p>	2003	<p>BACKGROUND: Beta-carotene has been shown to enhance immune functions in humans. Whether vegetables rich in carotenoids, such as beta-carotene or lycopene, modulate immune functions in healthy humans is presently not known. The objective of this study was to investigate the effects of a low-carotenoid diet supplemented with either tomato (providing high amounts of lycopene) or carrot juice (providing high amounts of alpha- and beta-carotene) on immune functions in healthy men. METHOD: In a blinded, randomized, cross-over study, male subjects on a low-carotenoid diet consumed 330 ml/day of either tomato juice (37.0 mg/day lycopene) or carrot juice (27.1 mg/day beta-carotene and 13.1 mg/day alpha-carotene) for 2 weeks with a 2-week depletion period after juice intervention. Immune status was assessed by measuring lytic activity of natural killer (NK) cells, secretion of cytokines (IL-2, IL-4,</p>	RCT

				<p>TNFalpha), and proliferation by activated peripheral blood mononuclear cells.</p> <p>RESULTS: Juice consumption resulted in relatively fast responses in plasma carotenoid concentrations (<math>p &lt; 0.0002</math>) which were not accompanied by concomitant changes in immune functions. For IL-2, NK cell cytotoxicity, and lymphocyte proliferation, maximum responses were observed during depletion periods. The highest production rate was measured only for TNFalpha at the end of the first intervention period. Juice intervention did not modulate the secretion of IL-4.</p> <p>CONCLUSIONS: Increased plasma carotenoid concentrations after vegetable juice consumption are accompanied by a time-delayed modulation of immune functions in healthy men consuming a low-carotenoid diet.</p>	
CVD: oxidation	Briviba K	<p>Effects of supplementing a low-carotenoid diet with a tomato extract for 2 weeks on endogenous levels of DNA single strand breaks and immune functions in healthy non-smokers and smokers.</p> <p>Briviba K, Kulling SE, Moseneder J, Watzl B, Rechkemmer G, Bub A.</p> <p>Carcinogenesis. 2004 Dec;25(12):2373-8. Epub 2004 Aug 12.</p>	2004	<p>Increased consumption of tomato products is associated with a decreased risk of cancer. The present study was performed to investigate whether consumption of a tomato oleoresin extract for 2 weeks can affect endogenous levels of DNA single strand breaks in peripheral blood lymphocytes in healthy non-smokers and smokers. We also assessed, the effect of the tomato oleoresin extract on various immunological functions of peripheral blood mononuclear cells. A double-blinded, randomized, placebo-controlled study design was used. Over a period of 2 weeks 15 non-smokers and 12 smokers were given three tomato oleoresin extract capsules daily (each containing 4.88 mg lycopene, 0.48 mg phytoene, 0.44 mg phytofluene and 1.181 mg alpha-tocopherol). The control group received placebos. The baseline level of endogenous DNA damage for non-smokers was slightly (13% ) and non-significantly (<math>P = 0.44</math>) lower than that of smokers. Placebo supplementation of non-smokers and smokers for 2 weeks did not significantly affect lycopene plasma levels or DNA damage in either group. Intervention with tomato oleoresin extract resulted in significant increases in total plasma lycopene and resulted in decreased levels of DNA strand breaks of approximately 32 (non-smokers) and 39% (smokers). However, this effect was not statistically significant in either group (<math>P = 0.09</math> for non-smokers and <math>P = 0.12</math> for smokers). Analysis of the distribution pattern of DNA strand breaks showed a statistically significant (<math>P &lt; 0.05</math>) increase in the number of comets in class 0 (undamaged) and a decrease in classes 1 and 2 (damaged) after the tomato oleoresin extract intervention in non-smokers. The changes in the smoker group were not statistically significant. Treatment with the tomato</p>	RCT

				extract had no effect on lymphocyte proliferation, NK cell activity, interleukin (IL)-2 production and tumor necrosis factor (TNF)alpha production, but it significantly reduced IL-4 production in smokers (P = 0.009).	
CVD: oxidation	Briviba K	Supplementation of a diet low in carotenoids with tomato or carrot juice does not affect lipid peroxidation in plasma and feces of healthy men.  Briviba K, Schnabele K, Rechkemmer G, Bub A.  J Nutr. 2004 May;134(5):1081-3.	2004	Antioxidant properties of carotenoids are thought to be at least partly responsible for the protective effects of fruits and vegetables rich in carotenoids against colon cancer. There are large amounts of in vitro data supporting this hypothesis. But there is little known about the antioxidant effects of carotenoid-rich food in vivo particularly in the gastrointestinal tract. In a randomized, crossover trial, healthy men (n = 22) who were consuming a low-carotenoid diet drank 330 mL/d tomato juice or carrot juice for 2 wk. Antioxidant capacity was assessed by the "lag time" of ex vivo LDL oxidation induced by copper and lipid peroxidation as determined by measurements of malondialdehyde (MDA) in plasma and feces using HPLC with fluorescence detection. Although consumption of both carotenoid-rich juices for 2 wk increased the carotenoid level in plasma and feces (P < 0.001), the antioxidant capacity of LDL tended to be increased by only approximately 4.5% (P = 0.08), and lipid peroxidation in the men's plasma and feces was not affected. Thus, processes other than lipid peroxidation could be responsible for the preventive effects of tomatoes and carrots against colon cancer.	RCT
CVD: oxidation lipids	Collins JK	Lycopene from two food sources does not affect antioxidant or cholesterol status of middle-aged adults.  Collins JK, Arjmandi BH, Claypool PL, Perkins-Veazie P, Baker RA, Clevidence BA.  Nutr J. 2004 Sep 15;3:15.	2004	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.  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	RCT

				<p>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	Rao AV	<p>Processed tomato products as a source of dietary lycopene: bioavailability and antioxidant properties.</p> <p>Rao AV.</p> <p>Can J Diet Pract Res.2004 Winter;65(4):161-5.</p>	2004	<p>Oxidative stress is one of the major contributors to increased risk of chronic diseases. A diet rich in tomatoes and tomato products containing lycopene, a carotenoid antioxidant, has been found to protect against these chronic diseases by mitigating oxidative damage. The study aim was to evaluate the effects of a long-term tomato-rich diet, consisting of various processed tomato products, on bioavailability and antioxidant properties of lycopene. Seventeen healthy human subjects (ten men, seven non-pregnant women) participated in the study. Following a two-week washout period during which subjects avoided foods containing lycopene, all subjects consumed test tomato products including tomato juice, tomato sauce, tomato paste, ketchup, spaghetti sauce, and ready-to-serve tomato soup providing 30 mg of lycopene a day for four weeks. At the end of treatment, serum lycopene level increased significantly (<math>p &lt; 0.05</math>), from 181.79 +/- 31.25 to 684.7 +/- 113.91 nmol/L. Similarly, total antioxidant potential increased significantly (<math>p &lt; 0.05</math>), from 2.26 +/- 0.015 to 2.38 +/- 0.17 mmol/L Trolox equivalent. Lipid and protein oxidation was reduced significantly (<math>p &lt; 0.05</math>). The results suggest that a tomato-rich diet containing different sources of lycopene can increase serum lycopene levels and reduce oxidative stress effectively.</p>	Interv
CVD: oxidation	Riso P	<p>Lycopene and vitamin C concentrations increase in plasma and lymphocytes after</p>	2004	<p>OBJECTIVE: This study seeks to verify whether the regular consumption of small amounts of tomato products can protect lymphocyte DNA and lipids from oxidative damage.</p>	Interv

		<p>tomato intake. Effects on cellular antioxidant protection.</p> <p>Riso P, Visioli F, Erba D, Testolin G, Porrini M.</p> <p>Eur J Clin Nutr.2004 Oct;58(10):1350-8.</p>		<p>DESIGN: Standardized dietary intervention.SUBJECTS: Twelve healthy female subjects (mean age 25.2 y).INTERVENTION: Subjects were instructed to follow a standardized diet for 1 week, followed by 3 weeks consumption of the same diet enriched with small amounts of different tomato products providing as a mean 8 mg lycopene, 0.5 mg beta-carotene and 11 mg vitamin C per day. Plasma and lymphocyte concentrations of carotenoids, vitamin C and vitamin E were analysed. Ex vivo protection of lymphocyte DNA from oxidative injury produced by iron ions was evaluated by means of the Comet assay, and lipid peroxidation by HPLC analysis of malondialdehyde (MDA).</p> <p>RESULTS: Dietary intervention with tomato products increased lycopene concentration both in plasma (P &lt; 0.001) and lymphocytes (P &lt; 0.01). Vitamin C concentrations increased by approximately 35% in plasma (P &lt; 0.05) and by approximately 230% in lymphocytes (P &lt; 0.005). Vitamin E decreased significantly in plasma (P &lt; 0.0001) but not in lymphocytes. Finally, there was an improved protection from DNA oxidative damage (P &lt; 0.05) with no significant effect on MDA levels.</p> <p>CONCLUSIONS: Our results suggest that tomato products are not only good sources of lycopene but also sources of bioavailable vitamin C. A Regular intake of small amounts of tomato products can increase cell protection from DNA damage induced by oxidant species. This effect may originate from the synergism of different antioxidants present in tomatoes.</p>	
CVD: oxidation	Tyssandier V	<p>Effect of tomato product consumption on the plasma status of antioxidant microconstituents and on the plasma total antioxidant capacity in healthy subjects.</p> <p>Tyssandier V, Feillet-Coudray C, Caris-Veyrat C, Guillard JC, Coudray C, Bureau S, Reich M, Amiot- Carlin MJ, Bouteloup-Demange C, Boirie Y, Borel P.</p>	2004	<p>OBJECTIVES: to identify the plasma antioxidant microconstituents mainly affected by tomato product consumption, to check whether tomato product consumption can affect antioxidant status, and to identify tomato-product antioxidant-microconstituents mainly involved in the effect of these products on oxidative stress.</p> <p>DESIGN: Medium-term dietary supplementation study.SETTING: Human Nutrition Laboratory, Clermont-Ferrand, France.SUBJECTS: Twenty healthy young (20 &lt; years &lt; 40), non obese (18 &lt; BMI (kg/m2) &lt; 25), females were recruited by advertisement. All of them completed the study.INTERVENTION: The usual diet of the subjects was supplemented for three weeks with 96 g/day tomato puree. The volunteers then avoided tomato-product-rich foods for a subsequent three-week period. Measures of Outcome: Fasting blood samples were collected the day before</p>	Interv



		J Am Coll Nutr.2004 Apr;23(2):148-56.		<p>supplementation, the day after the supplementation period, and the day after the depletion period. The status of several antioxidant microconstituents (plasma microconstituent concentrations), and the antioxidant status (plasma total antioxidant capacity) were assessed.</p> <p>RESULTS: Supplementation with tomato puree significantly increased plasma lycopene, beta-carotene and lutein. Conversely it did not significantly affect plasmavitamin C and E, plasma antioxidant trace metals (Cu, Zn and Se), and plasma total antioxidant capacity. Avoidance of tomato-product-rich foods for three weeks significantly (<math>p &lt; 0.05</math>) decreased plasma lycopene, beta-carotene, lutein and vitamin C, as well as plasma total antioxidant capacity. Plasma total antioxidant capacity, as measured by chemiluminescence, was positively related (<math>p &lt; 0.05</math>) to the status of lycopene, vitamin C and beta-carotene.</p> <p>CONCLUSIONS: Tomato product consumption can affect not only the lycopene status, but also that of other antioxidant microconstituents (beta-carotene and lutein). Lycopene, but also beta-carotene, are apparently the main tomato microconstituents responsible for the effect of tomato products on antioxidant status.</p>	
CVD: oxidation	Bub A	<p>Paraoxonase 1 Q192R (PON1-192) polymorphism is associated with reduced lipid peroxidation in healthy young men on a low-carotenoid diet supplemented with tomato juice.</p> <p>Bub A, Barth SW, Watzl B, Briviba K, Rechkemmer G.</p> <p>Br J Nutr. 2005 Mar;93(3):291-7.</p>	2005	<p>The HDL-bound enzyme paraoxonase (PON) protects LDL from oxidation and may therefore attenuate the development of atherosclerosis. We examined the effect of tomato and carrot juice consumption on PON1 activity and lipid peroxidation in healthy young volunteers with different PON1-192 genotypes (Q/R substitution at position 192). In this randomized cross-over study twenty-two healthy, non-smoking men on a low-carotenoid diet received 330 ml/d tomato juice (37.0 mg lycopene, 1.6 mg beta-carotene) or carrot juice (27.1 mg beta-carotene, 13.1 mg alpha-carotene) for 2 weeks. Intervention periods were preceded by 2-week low-carotenoid intake. We determined the PON1-192 genotype by restriction fragment length polymorphism-polymerase chain reaction (RFLP-PCR) and measured ex vivo LDL oxidation (lag time), plasma malondialdehyde and PON1 activity at the beginning and end of each intervention period. At baseline, lag time was higher (<math>P &lt; 0.05</math>) in QQ (111 (sd 9) min) than in QR/RR subjects (101 (sd 8) min). Neither tomato nor carrot juice consumption had significant effects on PON1 activity. However, tomato juice consumption reduced (<math>P &lt; 0.05</math>) plasma malondialdehyde in QR/RR (Delta: -0.073 (sd 0.11) micromol/l) as compared to QQ subjects (Delta: +0.047 (sd 0.13) micromol/l). Carrot juice had no significant effect on malondialdehyde irrespective of the PON1-</p>	RCT

				192 genotype. Male volunteers with the QR/RR genotype showed an increased lipid peroxidation at baseline. Although tomato and carrot juice fail to affect PON1 activity, tomato juice intake reduced lipid peroxidation in healthy volunteers carrying the R-allele of the PON1-192 genotype and could thus contribute to CVD risk reduction in these individuals.	
CVD: oxidation	Porrini M	Daily intake of a formulated tomato drink affects carotenoid plasma and lymphocyte concentrations and improves cellular antioxidant protection.  Porrini M, Riso P, Brusamolino A, Berti C, Guarnieri S, Visioli F.  Br J Nutr. 2005 Jan;93(1):93-9.	2005	The salutary characteristics of the tomato are normally related to its content of carotenoids, especially lycopene, and other antioxidants. Our purpose was to verify whether the daily intake of a beverage prototype called Lyc-o-Mato((R)) containing a natural tomato extract (Lyc-o-Mato((R)) oleoresin 6 % ) was able to modify plasma and lymphocyte carotenoid concentrations, particularly those of lycopene, phytoene, phytofluene and beta-carotene, and to evaluate whether this intake was sufficient to improve protection against DNA damage in lymphocytes. In a double-blind, cross-over study, twenty-six healthy subjects consumed 250 ml of the drink daily, providing about 6 mg lycopene, 4 mg phytoene, 3 mg phytofluene, 1 mg beta-carotene and 1.8 mg alpha-tocopherol, or a placebo drink. Treatments were separated by a wash-out period. Plasma and lymphocyte carotenoid and alpha-tocopherol concentrations were determined by HPLC, and DNA damage by the comet assay. After 26 d of consumption of the drink, plasma carotenoid levels increased significantly: concentrations of lycopene were 1.7-fold higher (P<0.0001); of phytofluene were 1.6-fold higher (P<0.0001); of phytoene were doubled (P<0.0005); of beta-carotene were 1.3-fold higher (P<0.05). Lymphocyte carotenoid concentrations also increased significantly: that of lycopene doubled (P<0.001); that of phytofluene was 1.8-fold higher (P<0.005); that of phytoene was 2.6-fold higher (P<0.005); that of beta-carotene was 1.5-fold higher (P<0.01). In contrast, the alpha-tocopherol concentration remained nearly constant. The intake of the tomato drink significantly reduced (by about 42 % ) DNA damage (P<0.0001) in lymphocytes subjected to oxidative stress. In conclusion, the present study supports the fact that a low intake of carotenoids from tomato products improves cell antioxidant protection.	RCT
CVD: oxidation lipids	Ahuja KD	Effects of olive oil and tomato lycopene combination on serum lycopene, lipid profile, and lipid oxidation.	2006	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.	Interv

		<p>Ahuja KD, Pittaway JK, Ball MJ.</p> <p>Nutrition. 2006 Mar;22(3):259-65. Epub 2006 Jan 18.</p>		<p><b>METHODS:</b> 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><b>RESULTS:</b> Significant increases (<math>P&lt;0.001</math>) in serum lycopene concentration on both diets were to similar final concentrations. Higher serum high-density lipoprotein cholesterol (<math>P&lt;0.01</math>), lower ratio of total cholesterol to high-density lipoprotein (<math>P&lt;0.01</math>), and lower triacylglycerols (<math>P&lt;0.05</math>) 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><b>CONCLUSIONS:</b> Serum lycopene level changes with dietary lycopene intake irrespective of 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.</p>	
CVD:lipids	Blum A	<p>Effects of tomatoes on the lipid profile.</p> <p>Blum A, Merei M, Karem A, Blum N, Ben-Arzi S, Wirsansky I, Khazim K.</p> <p>Clin Invest Med. 2006 Oct;29(5):298-300.</p>	2006	<p><b>PURPOSE:</b> 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><b>METHODS:</b> 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><b>RESULTS:</b> 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; <math>P=0.33</math>), total cholesterol level (198.3+/-41.2mg/dl vs. 204.2+/-70.9mg/dl; <math>P=0.23</math>), HDL-cholesterol level (50.6+/-12.2mg/dl vs. 47.6+/-10.8mg/dl; <math>P=0.79</math>), and LDL-cholesterol level (122.7+/-39.4mg/dl vs. 120.2+/-32.2mg/dl; <math>P=0.24</math>) before</p>	Interv

				<p>and after the 1 month offollow-up. In the tomato-rich diet group: triglyceride level170.8+/-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>	
CVD: oxidation Lipids HgA1c	Bose KS	<p>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.</p> <p>Bose KS, Agrawal BK.</p> <p>West Indian Med J. 2006 Sep;55(4):274-8.</p>	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 &lt; 0.001). Likewise, significantly higher levels of lipid profile and glycated haemoglobin (HbA1c) in the diabetic group were observed when compared with control (p &lt; 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 &lt; 0.001), but there were no significant changes in lipid profile and glycated haemoglobin HbA1c levels (p &gt; 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.</p>	Interv
CVD: oxidation lipidsBP	Engelhard YN	<p>Natural antioxidants from tomato extract reduce blood pressure in patients with grade-1 hypertension: a double-blind, placebo-controlled pilot study.</p> <p>Engelhard YN, Gazer B, Paran E.</p> <p>Am Heart J. 2006 Jan;151(1):100.</p>	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, andoxidative stress markers.</p> <p>METHODS: This study is a single-blind, placebo-controlled trial. Thirty-one</p>	RCT

				<p>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 &lt; .001), and diastolic blood pressure decreased from 87.4 (SE +/- 1.2) to 83.4 mm Hg (SE +/- 1.2, P &lt; .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 &lt; .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>	
CVD: oxidation lipids	Madrid AE	<p>[Short-term Lycopodium consumption may increase plasma high density lipoproteins and decrease oxidative stress].</p> <p>[Article in Spanish] Madrid A E, Vásquez Z D, Leyton A F, Mandiola C, Escobar F JA.</p> <p>Rev Med Chil. 2006 Jul;134(7):855-62. Epub 2006 Aug 29.</p>	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. 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. SUBJECTS AND</p> <p>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 sample was drawn to measure total antioxidant capacity (TRAP), enzymatic antioxidants (catalase and superoxide dismutase), non-enzymatic antioxidants (lycopene and <math>\alpha</math>-tocopherol) and plasma lipoproteins.</p> <p>RESULTS: Lycopene level increased early and significantly in comparison with basal levels (48% ; p &lt; 0.05). TRAP, catalase and superoxide dismutase did not change significantly. HDL cholesterol increased significantly in 5.6 +/- 4.3 mg/dL (p &lt; 0.002) on the second sampling period,</p>	Interv

				<p>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.</p> <p>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.</p> <p>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 inTC (-24.2% ), LDL (-14.9% ) and HDL (+26.1% ). Triglyceride levels showed a smaller though significant increase at 6 months, butnot 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.</p> <p>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: platelet function	O'Kennedy N	<p>Effects of antiplatelet components of tomato extract on platelet function in vitro and ex vivo: a time-course cannulation study in</p>	2006	<p>BACKGROUND: Natural antithrombotic agents that influence platelet function are of potential interest for primary prevention of cardiovascular disease. Previous reports showed that tomato extracts inhibit platelet aggregation in vitro, but little is known of the active components, their</p>	Interv

		<p>healthy humans.</p> <p>O'Kennedy N, Crosbie L, van Lieshout M, Broom JI, Webb DJ, Duttaroy AK.</p> <p>Am J Clin Nutr. 2006 Sep;84(3):570-9.</p>		<p>mode of action, or their efficacy in vivo.</p> <p>OBJECTIVE: The objectives of the study were to examine the antiplatelet activity of specific tomato components by in vitro experimentation and to establish their ex vivo efficacy in healthy humans.</p> <p>DESIGN: The mechanisms of action of antiplatelet components isolated from tomato extracts were examined in vitro. A 7-h time-course study was carried out in cannulated human subjects (n = 23) to determine the ex vivo efficacy of a supplement drink containing tomato extract and the onset and duration of antiplatelet effects.</p> <p>RESULTS: The inhibition of ADP-, collagen-, thrombin-, and arachidonate-mediated platelet aggregation by tomato extract components appears to be linked to the inhibition of glycoprotein IIb/IIIa and platelet secretory mechanisms. We found a significant inhibition of baseline platelet function, from 2.9 +/- 1.4% (optimal ADP concentrations; P = 0.03) to 20.0 +/- 4.9% (suboptimal ADP concentrations; P &lt; 0.001), 3 h after supplementation with a dose of tomato extract equivalent to 6 tomatoes. The observed effects persisted for &gt;12 h. Coagulation variables were not affected.</p> <p>CONCLUSIONS: The ingestion of tomato components with in vitro antiplatelet activity significantly affects ex vivo platelet function. The reported cardioprotective effects of tomatoes are potentially linked to a modulation of platelet function.</p>	
CVD: platelet function	O'Kennedy N	<p>Effects of tomato extract on platelet function: a double-blinded crossover study in healthy humans.</p> <p>O'Kennedy N, Crosbie L, Whelan S, Luther V, Horgan G, Broom JI, Webb DJ, Duttaroy AK.</p> <p>Am J Clin Nutr. 2006 Sep;84(3):561-9.</p>	2006	<p>BACKGROUND: Aqueous extracts from tomatoes display a range of antiplatelet activities in vitro. We previously showed that the active components also alter ex vivo platelet function in persons with a high response to ADP agonist.</p> <p>OBJECTIVE: The objective was to evaluate the suitability of a tomato extract for use as a dietary supplement to prevent platelet activation.</p> <p>DESIGN: A randomized, double-blinded, placebo-controlled crossover study was conducted in 90 healthy human subjects selected for normal platelet function. Changes from baseline hemostatic function were measured 3 h after consumption of extract-enriched or control supplements.</p>	RCT

				<p>RESULTS: Significant reductions in ex vivo platelet aggregation induced by ADP and collagen were observed 3 h after supplementation with doses of tomato extract equivalent to 6 (6TE) and 2 (2TE) tomatoes [3 micromol ADP/L: 6TE (high dose), -21.3% ; 2TE (low dose), -12.7% ; P &lt; 0.001; 7.5 micromol ADP/L: 6TE, -7.8% , 2TE,-7.6% ; P &lt; 0.001; 3 mg collagen/L: 6TE, -17.5% ; 2TE, -14.6% ; P = 0.007]. No significant effects were observed for control supplements. A dose response to tomato extract was found at low levels of platelet stimulation. Inhibition of platelet function was greatest in a subgroup with the highest plasma homocysteine (P &lt; 0.05) and C-reactive protein concentrations (P &lt; 0.001).</p> <p>CONCLUSION: As a functional food or dietary supplement, tomato extract may have a role in primary prevention of cardiovascular disease by reducing platelet activation, which could contribute to a reduction in thrombotic events.</p>	
CVD: oxidation	Paterson E	<p>Supplementation with fruit and vegetable soups and beverages increases plasma carotenoid concentrations but does not alter markers of oxidative stress or cardiovascular risk factors.</p> <p>Paterson E, Gordon MH, Niwat C, George TW, Parr L, Waroonphan S, Lovegrove JA.</p> <p>J Nutr. 2006 Nov;136(11):2849-55.</p>	2006	<p>This study was aimed at determining whether an increase of 5 portions of fruits and vegetables in the form of soups and beverages has a beneficial effect on markers of oxidative stress and cardiovascular disease risk factors. The study was a single blind, randomized, controlled, crossover dietary intervention study. After a 2-wk run-in period with fish oil supplementation, which continued throughout the dietary intervention to increase oxidative stress, the volunteers consumed carotenoid-rich or control vegetable soups and beverages for 4 wk. After a 10-wk wash-out period, the volunteers repeated the above protocol, consuming the other intervention foods. Both test and control interventions significantly increased the % energy from carbohydrates and decreased dietary protein and vitamin B-12 intakes. Compared with the control treatment, consumption of the carotenoid-rich soups and beverages increased dietary carotenoids, vitamin C, alpha-tocopherol, potassium, and folate, and the plasma concentrations of alpha-carotene (362% ), beta-carotene (250% ) and lycopene (31% ) (P &lt; 0.01) and decreased the plasma homocysteine concentration by 8.8% (P &lt; 0.01). The reduction in plasma homocysteine correlated weakly with the increase in dietary folate during the test intervention (r = -0.35, P = 0.04). The plasma antioxidant status and markers of oxidative stress were not affected by treatment. Consumption of fruit and vegetable soups and beverages makes a useful contribution to meeting dietary recommendations for fruit and vegetable consumption.</p>	RCT



CVD: oxidation inflammation	Riso P	<p>Effect of a tomato-based drink on markers of inflammation, immunomodulation, and oxidative stress.</p> <p>Riso P, Visioli F, Grande S, Guarnieri S, Gardana C, Simonetti P, Porrini M.</p> <p>J Agric Food Chem. 2006 Apr 5;54(7):2563-6.</p>	2006	<p>Regular consumption of tomato and its products is being consistently associated with lower risk of several types of cancer and, to a lesser extent, coronary heart disease. Among the many tomato components credited with healthful properties, carotenoids and particularly lycopene are being actively investigated. Given the recognized role of immune/inflammatory processes in atherogenesis, the effects of a tomato-based drink (Lyc-o-Mato), which was previously shown to afford DNA protection from oxidative stress, on the modulation of immune and inflammatory markers (by enzyme immunoassay), on basal lymphocyte DNA damage (by comet assay), and on F2-isoprostane excretion (by LC-MS/MS), were investigated in 26 healthy youngvolunteers. In a placebo-controlled, double-blind, crossover study, Lyc-o-Mato (5.7 mg of lycopene, 3.7 mg of phytoene, 2.7 mg of phytofluene, 1 mg of beta-carotene, and 1.8 mg of alpha-tocopherol) or a placebo drink (same taste and flavor, but devoid of active compounds) were given for 26 days, separated by a wash-out period. During the study subjects maintained their habitual, hence unrestricted, diet. TNF-alpha production by whole blood was 34.4% lower after 26 days of drink consumption, whereas the other parameters were not significantly modified by the treatment. In turn, modest effects of the regular intake of a tomato drink, providing small amounts of carotenoids, were found on the production of inflammatory mediators, such as TNF-alpha, in young healthy volunteers. Future intervention trials in subjects with low carotenoid status and/or compromised immune system will resolve the issue of whether carotenoids modulate immune parameters in humans.</p>	RCT
CVD: oxidation inflammation	Sanchez- Moreno C	<p>Mediterranean vegetablesoup consumption increases plasma vitamin C and decreases F2-isoprostanes, prostaglandin E2 and monocyte chemot actic protein-1 in healthy humans.</p> <p>Sanchez-Moreno C, Cano MP, de Ancos B, Plaza L, Olmedilla B, Granado F, Martin A.</p> <p>J Nutr Biochem.2006 Mar;17(3):183-9. Epub 2005 Aug 15.</p>	2006	<p>Consumption of fruits and vegetables is associated with a reduced risk of death from all causes including heart disease and stroke. In this work, the bioavailability of vitamin C from a Mediterranean vegetable soup (gazpacho) constituted mainly of tomato, pepper and cucumber, and its influence on plasma vitamin C, 8-epi-prostaglandin F(2alpha) (8-epi-PGF2alpha), prostaglandin E2 (PGE2), monocyte chemotactic protein-1 (MCP-1), and the cytokines/tumor necrosis factor-alpha(TNF-alpha), interleukin-1beta (IL-1beta), and IL-6 concentrations in a healthy human population were assessed. Six menand six women consumed 500 ml of commercial gazpacho per day for 14 days, corresponding to an intake of 78 mg of ascorbic acid per day. There were no differences (P = .22) in baseline plasma vitamin C concentrations between the men and women. The maximum increase (P &lt; .05) in plasma vitamin C occurred 4 h postdose in both men and women. Vitamin Cconcentrations were significantly higher (P &lt; .03) on Days 7 and 14 of the intervention. Baseline</p>	Interv

				<p>concentrations of uric acid and 8-epi-PGF2alpha were significantly higher (<math>P &lt; \text{or} = .032</math>) in men than in women. Baseline concentrations of 8-epi-PGF2alpha decreased significantly (<math>P &lt; \text{or} = .05</math>) by Day 14 of the intervention. A significant inverse correlation was observed between vitamin C and 8-epi-PGF2alpha (<math>r = -.415</math>, <math>P = .049</math>). Baseline concentrations of PGF2 and MCP-1 were significantly higher (<math>P &lt; \text{or} = .025</math>) in men than in women but decreased significantly (<math>P &lt; \text{or} = .05</math>) by Day 14 of the intervention. No effect on TNF-alpha, IL-1beta and IL-6 was observed at Day 14 of the intervention. Drinking gazpacho (500 ml/day) significantly increases plasma concentrations of vitamin C and significantly decreases 8-epi-PGF2alpha, PGE2 and MCP-1 concentrations in healthy humans.</p>	
CVD: oxidation	Zhao X	<p>Modification of lymphocyte DNA damage by carotenoid supplementation in postmenopausal women.</p> <p>Zhao X, Aldini G, Johnson EJ, Rasmussen H, Kraemer K, Woolf H, Musaeus N, Krinsky NI, Russell RM, Yeum KJ.</p> <p>Am J Clin Nutr. 2006 Jan;83(1):163-9.</p>	2006	<p>BACKGROUND: Oxidative stress has been implicated in the pathogenesis of chronic diseases related to aging such as cancer and cardiovascular disease. Carotenoids could be a part of a protective strategy to minimize oxidative damage in vulnerable populations, such as the elderly.</p> <p>OBJECTIVE: Our aim was to determine the protective effect of carotenoids against DNA damage.</p> <p>DESIGN: A randomized, double-blind, placebo-controlled intervention study was conducted. Thirty-seven healthy, nonsmoking postmenopausal women aged 50-70 y were randomly assigned to 1 of 5 groups and were instructed to consume a daily dose of mixed carotenoids (beta-carotene, lutein, and lycopene; 4 mg each), 12 mg of a single carotenoid (beta-carotene, lutein, or lycopene), or placebo for 56 d. Plasma carotenoid concentrations were analyzed by using HPLC, and lymphocyte DNA damage was measured by using a single-cell gel electrophoresis (comet) assay.</p> <p>RESULTS: At day 57, all carotenoid-supplemented groups showed significantly lower endogenous DNA damage than at baseline (<math>P &lt; 0.01</math>), whereas the placebo group did not show any significant change. Significantly less (<math>P &lt; 0.05</math>) endogenous DNA damage was found as early as day 15 in the mixed carotenoid (<math>P &lt; 0.01</math>) and beta-carotene (<math>P &lt; 0.05</math>) groups.</p> <p>CONCLUSIONS: The results indicate that carotenoid supplementation decreases DNA damage and that a combination of carotenoids (4 mg each of lutein, beta-carotene, and lycopene), an intake that can be</p>	RCT

				achieved by diet, or a larger dose (12 mg) of individual carotenoids exerts protection against DNA damage.	
CVD: inflammation endothelial function markers	Blum A	Tomato-rich (Mediterranean) diet does not modify inflammatory markers.  Blum A, Monir M, Khazim K, Peleg A, Blum N.  Clin Invest Med. 2007;30(2):E70-4.	2007	<p>BACKGROUND: The Mediterranean diet is rich in lycopene and has been reported to reduce cardiovascular events. The mechanism of prevention of cardiovascular events has not been clearly established. Our aim was to study the effects of a tomatoes-rich diet on markers of vascular inflammation.</p> <p>METHODS: Plasma concentrations of E-selectin, intercellular adhesion molecule 1 (ICAM-1), and high sensitivity C-reactive protein (hs-CRP) were determined by ELISA in 103 apparently healthy volunteers. Volunteers were randomly assigned to two groups: 50 participants ate 300 g tomatoes daily for 1 month, and 53 participants ate their usual diet with tomatoes prohibited during that period. Markers of inflammation were measured before enrollment and 1 month after their assigned diet.</p> <p>RESULTS: The two diet groups had similar baseline clinical characteristics and similar baseline levels of inflammatory markers. After 30 days of assigned diet concentrations of hs-CRP, E-selectin and ICAM-1 were unchanged compared with baseline in the tomato-rich diet. However, ICAM-1 concentration was increased in the regular diet group from 247.55+/-55 ng/ml to 264.71+/-60.42 ng/ml (P=0.01).</p> <p>CONCLUSIONS: The mechanisms of benefit of the tomato-rich diet are not directly related to inhibition of markers of vascular inflammation</p>	RCT
CVD: oxidation lipids	Bose KS	Effect of lycopene from cooked tomatoes on serum antioxidant enzymes, lipid peroxidation rate and lipid profile in coronary heart disease.  Bose KS, Agrawal BK.  Singapore Med J. 2007 May;48(5):415-20.	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 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</p>	Interv

				<p>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	Neyestani TR	<p>Physiological dose of lycopene suppressed oxidative stress and enhanced serum levels of immunoglobulin M in patients with Type 2 diabetes mellitus: a possible role in the prevention of long-term complications.</p> <p>Neyestani TR, Shariatzadeh N, Gharavi A, Kalayi A, Khalaji N.</p> <p>J Endocrinol Invest. 2007 Nov;30(10):833-8.</p>	2007	<p>OBJECTIVE: This study was undertaken to evaluate the antioxidant effects of lycopene in physiological doses and its possible effects on the immune response in patients with Type 2 diabetes mellitus (T2DM). RESEARCH DESIGN AND</p> <p>METHODS: A total of 35 patients with T2DM of both sexes aged 54+/-9 yr were enrolled in a double-blind placebo-controlled clinical trial conducted for 2 months. After a 2-week lycopene-free diet washout period, patients were allocated to either lycopene supplementation group (10 mg/day) (no.=16) or placebo group (no.=19), which were age- and sex matched. Patients were instructed to keep their diet and physical activity as unchanged as possible.</p> <p>RESULTS: While dietary intake of energy and body weight did not change, the ratio of serum total antioxidant capacity (TAC) to malondialdehyde (MDA) increased significantly in the lycopene group compared to the placebo group (p=0.007). Though a statistically significant increase in serum concentrations of lycopene (p&lt;0.001) was not accompanied by enhanced delayed-type hypersensitivity response, a significant negative correlation was found between serum levels of lycopene and immunoglobulin (Ig)G (r=-0.338, p=0.008). Interestingly, variations of serum levels of lycopene directly correlated with those of IgM (r=0.466, p=0.005). There was an insignificant decrement in serum anti-oxidized LDL IgG levels in the lycopene group.</p> <p>CONCLUSIONS: Lycopene, probably by increasing TAC and inhibiting</p>	RCT

				MDA-LDL formation, may attenuate T cell-dependent adaptive (pro-atherogenic) immune response. Meanwhile, with enhancement of innate immunity and hence prevention of ox-LDL uptake by macrophage and foam cell formation, lycopene may be effective in prevention of long-term diabetic complications, notably cardiovascular disease.	
CVD: oxidation lipids	Shen YC	Contribution of tomato phenolics to antioxidation and down-regulation of blood lipids.  Shen YC, Chen SL, Wang CK.  J Agric Food Chem. 2007 Aug 8;55(16):6475-81. Epub 2007 Jul 13.	2007	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.	RCT
CVD: oxidation lipids	Silaste ML	Tomato juice decreases LDL cholesterol levels and increases LDL resistance to oxidation.  Silaste ML, Alfthan G, Aro A, Kesäniemi YA, Hörkkö S.  Br J Nutr. 2007 Dec;98(6):1251-8. Epub 2007 Jul 9.	2007	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 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	RCT

				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	Briviba K	No differences in DNA damage and antioxidant capacity between intervention groups of healthy, nonsmoking men receiving 2, 5, or 8 servings/day of vegetables and fruit.  Briviba K, Bub A, Moseneder J, Schwerdtle T, Hartwig A, Kulling S, Watzl B.  Nutr Cancer. 2008;60(2):164-70.	2008	The effects of different intake levels of vegetables and fruit (VF) on some cancer-relevant biomarkers such as DNA damage and oxidative stress were investigated. In a randomized controlled trial, 64 nonsmoking male subjects were asked to consume a diet with 2 servings of VF/day for 4 wk. Then subjects were randomly assigned to 1 of 3 groups with either a low (2 servings/day), medium (5 servings/day), or high (8 servings/day) intake level of VF for another 4 wk. At the end of study, the plasma lutein, zeaxanthin, alpha-carotene, and beta-carotene but not cryptoxanthin and lycopene concentrations were significantly higher in subjects consuming 8 servings/day than in those receiving 2 servings/day. Different levels of VF consumption and plasma carotenoid concentrations did not result in differences in the levels of endogenous DNA strand breaks, oxidative DNA damage, antigenotoxic capacity of lymphocytes, plasma markers for lipid peroxidation (malondialdehyde, 8-iso-prostaglandin-F2alpha) and antioxidant capacity [trolox-equivalent antioxidant capacity assay]. Thus, although consumption of 8 servings vs 2 servings/day of VF for 4 wk significantly increased the carotenoid level in plasma, there were no differences in DNA damage, lipid peroxidation, and antioxidant capacity markers among healthy, well-nourished, nonsmoking men.	RCT
CVD: oxidation inflammation endothelial function markers	Denniss SG	Effect of short-term lycopene supplementation and postprandial dyslipidemia on plasma antioxidants and biomarkers of endothelial health in young, healthy individuals.  Denniss SG, Haffner TD, Kroetsch JT, Davidson SR, Rush JW, Hughson RL.	2008	The objective of this study was to test the hypothesis that the effect of a high-fat meal (HFm) on plasma lipid-soluble antioxidants and biomarkers of vascular oxidative stress and inflammation would be attenuated by short-term lycopene supplementation in young healthy subjects. Following restriction of lycopene-containing foods for 1-wk (LYr), blood was collected in a fasting state and 3 h after a HFm and a low-fat meal (LFm) in N = 18 men aged 23 +/- 2 years, and after a HFm only in N = 9 women aged 23 +/- 1 years. Blood was also sampled pre- and post-meals following 1-wk of 80 mg/day lycopene supplementation (LYs) under continued dietary LYr. In the fasting state, LYs compared with LYr not only evoked a >2-fold increase in plasma lycopene but also increased plasma	Interv

		Vasc Health Risk Manag. 2008;4(1):213-22.		beta-carotene and alpha-tocopherol ( $p < 0.01$ ), though LYs did not affect plasma nitrate/nitrite (biomarker of nitric oxide), malondialdehyde (biomarker of lipid oxidative stress), vascular- and intercellular-adhesion molecules or C-reactive protein (biomarkers of inflammation). Contrary to the hypothesis, the HFm-induced dyslipidemic state did not affect plasma malondialdehyde, C-reactive protein, or adhesion molecules in either LYr or LYs. Both the HFm and LFM were associated with decreases in the nitric oxide metabolites nitrate/nitrite and lipid-soluble antioxidants ( $p < 0.05$ ). The data revealed that 1-wk of LYs increased plasma lycopene, beta-carotene, and alpha-tocopherol yet despite these marked changes to the plasma lipid-soluble antioxidant pool, biomarkers of vascular oxidative stress and inflammation were unaffected in the fasted state as well as during dyslipidemia induced by a HFm in young healthy subjects.	
CVD: oxidation	Devaraj S	A dose-response study on the effects of purified lycopene supplementation on biomarkers of oxidative stress.  Devaraj S, Mathur S, Basu A, Aung HH, Vasu VT, Meyers S, Jialal I.  J Am Coll Nutr. 2008 Apr;27(2):267-73.	2008	<p>OBJECTIVE: While tomato product supplementation, containing antioxidant carotenoids, including lycopene, decreases oxidative stress, the role of purified lycopene as an antioxidant remains unclear. Thus, we tested the effects of different doses of purified lycopene supplementation on biomarkers of oxidative stress in healthy volunteers.</p> <p>METHODS: This was a double-blind, randomized, placebo-controlled trial, examining the effects of 8-week supplementation of purified lycopene, on plasma lycopene levels, biomarkers of lipid peroxidation {LDL oxidizability, malondialdehyde &amp; hydroxynonenals (MDA &amp; HNE), urinary F(2)-isoprostanes}, and markers of DNA damage in urine and lymphocytes. Healthy adults (<math>n = 77</math>, age <math>\geq 40</math> years), consumed a lycopene-restricted diet for 2 weeks, and were then randomized to receive 0, 6.5, 15, or 30 mg lycopene/day for 8 weeks, while on the lycopene-restricted diet. Blood and urine samples were collected at the beginning and end of Week 2 of lycopene-restricted diet, and at end of Week 10 of the study.</p> <p>RESULTS: Independent of the dose, plasma lycopene levels significantly increased in all lycopene supplemented groups versus placebo (<math>p &lt; 0.05</math>). ANOVA revealed a significant decrease in DNA damage by the comet assay (<math>p = 0.007</math>), and a significant decrease in urinary 8-hydroxy deoxoguanosine (8-OHdG) at 8 weeks versus baseline (<math>p = 0.0002</math>), with 30 mg lycopene/day. No significant inter- or intra-group differences were noted for glucose, lipid profile, or other biomarkers of lipid peroxidation at any dose/time point.</p>	RCT

				CONCLUSIONS: Thus, purified lycopene was bioavailable and was shown to decrease DNA oxidative damage and urinary8-OHdG at the high dose.	
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	Burri BJ	Tangerine tomatoes increase total and tetra-cis- lycopene isomer concentrations more than red tomatoes in healthy adult humans.  Burri BJ, Chapman MH, Neidlinger TR, Seo JS, Ishida BK.  Int J Food Sci Nutr. 2008 Apr 10;1-16. [Epub ahead of print]	2009	Lycopene, or the foods that contain it, may prevent prostate cancer. Studies suggest that some cis-lycopene isomers are more bioavailable than the trans-lycopene isomer. We hypothesized that tangerine tomatoes, which predominantly contain the tetra-cis isomer, should be a good source of bioavailable lycopene. We fed lunches containing 300 g tangerine or red tomato sauce per day to 21 healthy adults in a double-blind crossover design. We collected blood at baseline and after each treatment and washout period. We measured tetra-cis, other cis, and trans lycopene, as well as other carotenoids, by reversed-phase high-performance liquid chromatography. Both tomato sauces increased lycopene concentrations in blood, but the tangerine tomato sauce caused a greater increase of total and tetra-cis-lycopene. The cis isomer(s) may also have facilitated absorption of the trans-lycopene	RCT



				isomer. Indices of oxidative damage decreased as serum lycopene concentrations increased. Our results suggest that total lycopene concentrations can be increased by substituting tetra-cis-lycopene-rich tangerine tomatoes for common red tomatoes in the diet.	
CVD: oxidation	Lee CY	Limited antioxidant effect after consumption of a single dose of tomato sauce by young males, despite a rise in plasma lycopene.  Lee CY, Isaac HB, Huang SH, Long LH, Wang H, Gruber J, Ong CN, Kelly RP, Halliwell B.  Free Radic Res. 2009 Jun;43(6):622-8.	2009	This study investigated the effect of a single dose of tomato sauce on healthy male volunteers in a randomized crossover study. Healthy male subjects (n = 10) were enrolled. Placebo (rice and olive oil) or tomato (tomato sauce, rice and olive oil) meals were provided to the volunteers. Blood and urine samples were taken before consumption of meal (0 h) and 2, 4, 6, 24 and 48 h after meal. Consumption of tomato sauce increased plasma lycopene level by 5-22% , with a maximum level at 24 h (p<0.01) after the meal. Levels of plasma F(2)-isoprostanes, hydroxyeicosatetraenoic acid products, allantoin and urinary 8-hydroxy-2'-deoxyguanosine did not change after either meal, but urinary F(2)-isoprostanes (p<0.05) significantly decreased at 48 h compared to 0 h after the tomato sauce meal. This study showed that a single dose of tomato sauce meal had only a limited antioxidant effect in vivo.	RCT
CVD: oxidation inflammation	Markovits N	The effect of tomato-derived lycopene on low carotenoids and enhanced systemic inflammation and oxidation in severe obesity.  Markovits N, Ben Amotz A, Levy Y.  Isr Med Assoc J. 2009 Oct;11(10):598-601.	2009	BACKGROUND: Fat tissue mediates the production of inflammatory cytokines and oxidative products, which are key steps in the development of type 2 diabetes and atherosclerosis. Antioxidant-rich diets protect against chronic diseases. Antioxidants may interfere with pro-inflammatory signals.  OBJECTIVES: To investigate the effect of the potent tomato-derived antioxidant carotenoid, lycopene, on plasma antioxidants (carotenoids and vitamin E), inflammatory markers (C-reactive protein, interleukin-6, tumor necrosis factor-alpha) and oxidation products (conjugated dienes).  METHODS: Eight obese patients (body mass index 37.5 +/- 2.5 kg/m <sup>2</sup> ) were compared with a control group of eight lean, age and gender-matched subjects (BMI 21.6 +/- 0.6 kg/m <sup>2</sup> ), before and after 4 weeks of lycopene supplementation (tomato-derived Lyc-O-Mato) (30 mg daily).  RESULTS: Plasma carotenoids were significantly reduced in the obese compared to control subjects (0.54 +/- 0.06 vs. 0.87 +/- 0.08 microg/ml, P < 0.01). CRP levels were significantly higher (6.5 vs. 1.1 mg/L, P = 0.04) in obese vs. controls, as were IL-6 and conjugated dienes (3.6 and 7.9-fold, respectively). CRP, IL-6 and conjugated dienes correlated with BMI, while	Interv

				<p>IL-6 and conjugated dienes correlated inversely with carotenoids (<math>P &lt; 0.05</math>). Following lycopene treatment, a significant elevation of plasma carotenoids (1.79 vs. 0.54 microg/ml) and specifically lycopene (1.15 vs 0.23 microg/ml) (<math>P &lt; 0.001</math>) occurred in the treatment vs. the placebo group, respectively. Markers of inflammation and oxidation products were not altered by lycopene.</p> <p>CONCLUSIONS: Obese patients showed abnormally higher markers of inflammation and oxidation products and lower plasma carotenoids. The lack of reduction of pro-inflammatory markers could be attributed to the short period of the study and the small number of participants. More studies are needed on the protective qualities of natural antioxidant-rich diets against obesity-related co-morbidities.</p>	
CVD: BP	Paran E	<p>The effects of natural antioxidants from tomato extract in treated but uncontrolled hypertensive patients.</p> <p>Paran E, Novack V, Engelhard YN, Hazan-Halevy I.</p> <p>Cardiovasc Drugs Ther. 2009 Apr;23(2):145-51. Epub 2008 Dec 4</p>	2009	<p>PURPOSE: To evaluate the effect of adding tomato extract to the treatment regime of moderate hypertensives with uncontrolled blood pressure (BP) levels.</p> <p>METHODS: Fifty four subjects with moderate HT treated with one or two antihypertensive drugs were recruited and 50 entered two double blind cross-over treatment periods of 6 weeks each, with standardized tomato extract or identical placebo. Plasma concentrations of lycopene, nitrite and nitrate were measured and correlated with BP changes.</p> <p>RESULTS: There was a significant reduction of systolic BP after 6 weeks of tomato extract supplementation, from 145.8 +/- 8.7 to 132.2 +/- 8.6 mmHg (<math>p &lt; 0.001</math>) and 140.4 +/- 13.3 to 128.7 +/- 10.4 mmHg (<math>p &lt; 0.001</math>) in the two groups accordingly. Similarly, there was a decline in diastolic BP from 82.1 +/- 7.2 to 77.9 +/- 6.8 mmHg (<math>p = 0.001</math>) and from 80.1 +/- 7.9 to 74.2 +/- 8.5 mmHg (<math>p = 0.001</math>). There was no significant change in systolic and diastolic BP during the placebo period. Serum lycopene level increased from 0.11 +/- 0.09 at baseline, to 0.30 +/- 0.13 micromol/L after tomato extract therapy (<math>p &lt; 0.001</math>). There was a significant correlation between systolic BP and lycopene levels (<math>r = -0.49</math>, <math>p &lt; 0.001</math>).</p> <p>CONCLUSIONS: Tomato extract when added to patients treated with low doses of ACE inhibition, calcium channel blockers or their combination with low dose diuretics, had a clinically significant effect-reduction of BP by more than 10 mmHg systolic and more than 5 mmHg diastolic pressure. No side-effects to treatment were recorded and the compliance with treatment was high. The significant correlation between systolic blood</p>	RCT

				pressure values and level of lycopene suggest the possibility of cause-effect relationships.	
CVD: BP	Ried K	<p>Dark chocolate or tomato extract for prehypertension: a randomised controlled trial.</p> <p>Ried K, Frank OR, Stocks NP.</p> <p>BMC Complement Altern Med. 2009 Jul 8;9:22</p>	2009	<p>BACKGROUND: Flavanol-rich chocolate and lycopene-rich tomato extract have attracted interest as potential alternative treatment options for hypertension, a known risk factor for cardiovascular morbidity and mortality. Treatment of prehypertension (SBP 120-139/DBP 80-89 mmHg) may forestall progression to hypertension. However, there has been only limited research into non-pharmacological treatment options for prehypertension. We investigated the effect of dark chocolate or tomato extract on blood pressure, and their acceptability as an ongoing treatment option in a prehypertensive population.</p> <p>METHODS: Our trial consisted of two phases: a randomised controlled three-group-parallel trial over 12 weeks (phase 1) followed by a crossover of the two active treatment arms over an additional 12-week period (phase 2). Group 1 received a 50 g daily dose of dark chocolate with 70% cocoa containing 750 mg polyphenols, group 2 were allocated one tomato extract capsule containing 15 mg lycopene per day, and group 3 received one placebo capsule daily over 8 weeks followed by a 4-week washout period. In phase 2 the active treatment groups were crossed over to receive the alternative treatment. Median blood pressure, weight, and abdominal circumference were measured 4-weekly, and other characteristics including physical activity, general health, energy, mood, and acceptability of treatment were assessed by questionnaire at 0, 8 and 20 weeks. We analysed changes over time using a linear mixed model, and one time point differences using Kruskal-Wallis, Fisher's-Exact, or t-tests.</p> <p>RESULTS: Thirty-six prehypertensive healthy adult volunteers completed the 6-month trial. blood pressure changes over time within groups and between groups were not significant and independent of treatment. Weight and other characteristics did not change significantly during the trial. However, a marked difference in acceptability between the two treatment forms (chocolate or capsule) was revealed (<math>p &lt; 0.0001</math>). Half of the participants allocated to the chocolate treatment found it hard to eat 50 g of dark chocolate every day and 20% considered it an unacceptable long-term treatment option, whereas all participants found it easy and acceptable to take a capsule each day for blood pressure.</p> <p>CONCLUSION: Our study did not find a blood pressure lowering effect of</p>	RCT

				dark chocolate or tomato extract in a prehypertensive population. Practicability of chocolate as a long-term treatment option may be limited.	
CVD: oxidation lipids	Talvas J	<p>Differential effects of lycopene consumed in tomato paste and lycopene in the form of a purified extract on target genes of cancer prostatic cells.</p> <p>Talvas J, Caris-Veyrat C, Guy L, Rambeau M, Lyan B, Minet-Quinard R, Lobaccaro JM, Vasson MP, Georgé S, Mazur A, Rock E.</p> <p>Am J Clin Nutr. 2010 Jun;91(6):1716-24. Epub 2010Apr 14</p>	2010	<p>BACKGROUND: Prospective studies indicate that tomato consumers are protected against prostate cancer. Lycopene has been hypothesized to be responsible for tomato health benefits.</p> <p>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.</p> <p>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 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 <a href="http://www.sante-sports.gouv.fr">http://www.sante-sports.gouv.fr</a> as 2006-A00396-45.</p>	RCT

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 (<math>\geq 100</math> 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 (<math>P&lt;.0001</math>) and <math>\beta</math>-carotene (<math>P&lt;.0001</math>), while plasma lycopene was reduced (<math>P&lt;.05</math>) after 12 weeks. Low-density lipoprotein cholesterol was reduced from <math>138\pm 35</math> to <math>114\pm 33</math> mg/dl (<math>P&lt;.0001</math>). In addition, decreases were observed in the atherogenic subfractions: large very low-density lipoprotein (<math>P&lt;.05</math>), small LDL (<math>P&lt;.00001</math>) and medium high-density lipoprotein (<math>P&lt;.05</math>), oxidized LDL was significantly reduced by 12% in both groups (<math>P&lt;.01</math>). Changes in OxLDL were inversely correlated with plasma lutein (<math>r=-.478</math>, <math>P&lt;.0001</math>). 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 functionBP	Kim JY	<p>Effects of lycopene supplementation on oxidative stress and markers of endothelial function in 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>	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> <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 (<math>P&lt;0.001</math>). The 15 mg/day group had greater increase in plasma SOD activity (<math>P=0.014</math>) and reduction in lymphocyte DNA comet tail length (<math>P=0.042</math>) than the placebo group. Intragroup comparison revealed a 23% increase in RH-PAT index from baseline (<math>1.45\pm 0.09</math> vs. <math>1.79\pm 0.12</math>; <math>P=0.032</math>) in the 15 mg/day group after 8-week. hs-CRP, systolic blood pressure, sICAM-1 and sVCAM-1 significantly decreased, and <math>\beta</math>-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</p>	RCT

				<p>cell function at initial level. Changes in RH-PAT index correlated with SOD activity (<math>r=0.234</math>, <math>P=0.017</math>) especially in the 15 mg lycopene/day group (<math>r=0.485</math>, <math>P=0.003</math>), lymphocyte DNA comet tail moment (<math>r=-0.318</math>, <math>P=0.001</math>), and hs-CRP (<math>r=-0.238</math>, <math>P=0.011</math>). In addition, changes in lycopene correlated with hs-CRP (<math>r=-0.230</math>, <math>P=0.016</math>) and SOD activity (<math>r=0.205</math>, <math>P=0.037</math>).</p> <p>CONCLUSION: An increase in serum lycopene after supplementation can reduce oxidative stress which may play a role in endothelial function</p>	
CVD: oxidation	Martínez-Tomás R	<p>Effect of the consumption of a fruit and vegetable soup with high in vitro carotenoid bioaccessibility on serum carotenoid concentrations and markers of oxidative stress in young men.</p> <p>Martínez-Tomás R, Larqué E, González-Silvera D, Sánchez-Campillo M, Burgos MI, Wellner A, Parra S, Bialek L, Alminger M, Pérez-Llamas F.</p> <p>Eur J Nutr. 2011 Jun 7. [Epub ahead of print]</p>	2011	<p>AIM: To evaluate the effect of the daily intake of a fruit &amp; vegetable soup with high in vitro bioaccessibility of carotenoids on <math>\beta</math>-carotene and lycopene serum concentrations.</p> <p>METHODS: Fourteen healthy young men (<math>24 \pm 1</math> years) received 300 mL/day of a carrot, tomato, and broccoli soup, containing 3.9 mg <math>\beta</math>-carotene and 4 mg lycopene, for 4 weeks followed by a 4-week washout period. The serum carotenoid response and oxidative markers were analyzed after 3 and 4 weeks of soup consumption and after a 4-week washout.</p> <p>RESULTS: The in vitro bioaccessibility of <math>\beta</math>-carotene and lycopene was 55 and 43% , respectively, in the soup. Serum <math>\beta</math>-carotene concentrations were significantly higher than baseline (<math>0.33 \pm 0.05 \mu\text{mol/L}</math>) after 3 weeks (<math>0.69 \pm 0.06 \mu\text{mol/L}</math>) and 4 weeks (<math>0.78 \pm 0.10 \mu\text{mol/L}</math>) of soup consumption (<math>P &lt; 0.001</math>). Serum lycopene was also significantly higher compared with baseline levels (<math>0.26 \pm 0.08</math>-<math>0.56 \pm 0.04 \mu\text{mol/L}</math> and <math>0.60 \pm 0.04 \mu\text{mol/L}</math>, after 3 and 4 weeks, respectively) (<math>P &lt; 0.001</math>). Although the highest concentration of both carotenoids was found after 4 weeks, the levels were not statistically different from the levels at 3 weeks. A 4-week washout significantly decreased serum carotenoid concentrations, although only <math>\beta</math>-carotene returned to baseline. Glutathione peroxidase (GPx) increased significantly after soup supplementation compared with baseline, while superoxide dismutase was significantly lower only after 3 weeks. Glutathione reductase, lipid, protein, and DNA oxidative markers remained unchanged.</p> <p>CONCLUSIONS: The soup contributed to increasing the concentration of each carotenoid by more than 100% after 3 and 4 weeks of consumption, the maximum increase being observed after 4 weeks. Oxidative markers did not show any variation except for GPx. Serum lycopene half-life was</p>	Interv

				longer than that of $\beta$ -carotene, which may be important for studies evaluating both carotenoids.	
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 2010Dec 8.</p>	2011	<p>Tomatoes are a rich source of lycopene, <math>\beta</math>-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 type2 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: endothelial function	Stangl V	<p>Lack of effects of tomato products on endothelial function in human subjects: results of a randomised, placebo-controlled cross-over study.</p> <p>Stangl V, Kuhn C, Hentschel S, Jochmann N, Jacob C, Böhm V, Fröhlich K, Müller L, Gericke C, Lorenz M.</p> <p>Br J Nutr. 2011 Jan;105(2):263-7. Epub 2010 Aug 24.</p>	2011	<p>Epidemiological studies suggest that consumption of tomato products reduces the risk of CVD via antioxidant, hypocholesterolaemic and anti-inflammatory mechanisms. Although experimental data also describe beneficial effects on endothelial function, clinical data in human subjects are lacking. To test the hypothesis that tomato ingestion ameliorates endothelial function, we randomised healthy non-smoking postmenopausal women to consume a buttered roll with and without tomato purée (70 g) in a cross-over design. Endothelial-dependent flow-mediated dilation (FMD) and endothelial-independent nitro-mediated dilation of the brachial artery were assessed with high-resolution ultrasound (13 MHz linear array transducer). Acute (24 h) and long-term (7 d) effects were examined after daily consumption of the described meal. Nineteen volunteers completed the protocol and provided technically suitable ultrasound measurement data. Plasma lycopene levels increased from 0.30 (sem 0.04) (baseline) to 0.42 (sem 0.04) and to 0.74 (sem 0.06) <math>\mu</math>m after 24 h and 7 d, respectively, with tomato purée consumption. These data indicated an effective absorption of the tomato product. However, both acute and long-term tomato purée consumption had no effects on endothelium-dependent or -independent dilation of the brachial artery. In addition, we found no correlation between lycopene</p>	RCT

				plasma levels and FMD. In conclusion, consumption of tomato products associated with a significant increase in plasma lycopene levels had no effects on endothelial function in healthy postmenopausal women.	
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> <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>	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. METHODS AND</p> <p>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 &lt; 0.05). A trend for higher triglycerides at &gt;240 min was observed after the tomato meal (p = 0.006). Tomato significantly attenuated high-fat meal-induced LDL oxidation (p &lt; 0.05) and rise in interleukin-6 (p &lt; 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>	RCT
CVD: lipids inflammation BP insulin resistance endothelial function	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>	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.</p> <p>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.</p>	RCT



		Am J Clin Nutr. 2012 May;95(5):1013-22. doi:10.3945/ajcn.111.026286. Epub 2012 Apr 4.		<p>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.</p> <p>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.</p> <p>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>	
CVD: oxidation endothelial function	Xanplanteris P	<p>Tomato paste supplementation improves endothelial dynamics and reduces plasma total oxidative status in healthy subjects.</p> <p>Xanplanteris P, Vlachopoulos C, Pietri P, Terentes-Printzios D, Kardara D, Alexopoulos N, Aznaouridis K, Miliou A, Stefanadis C.</p> <p>Nutr Res. 2012 May;32(5):390-4. doi:10.1016/j.nutres.2012.03.011. Epub 2012 May 15.</p>	2012	<p>Consumption of tomato products is linked to beneficial outcomes through antioxidant and anti-inflammatory mechanisms. The aim of this study was to determine whether a 14-day period of tomato paste supplementation would improve endothelial function. Nineteen volunteers (mean age, 39 ± 13 years; 8 men/11 women) were studied in a randomized (exposure sequence), single-blind (operator), crossover design. The study consisted of a supplementation arm (70 g tomato paste containing 33.3 mg of lycopene) and a control arm, during which no tomato paste was added to their regular diet. Volunteers maintained their regular diet during study arms. Two-week washout periods preceded each arm. Flow-mediated dilatation (FMD) measured by brachial artery ultrasonography was used as an estimate of endothelial function at day 1 (acute response) and day 15 (midterm response). Plasma lipid peroxides were measured with a photometric enzyme-linked immunosorbent assay as an index of total oxidative status. Tomato supplementation led to an overall FMD increase compared with the control period (P = .047 for repeated-measures 3 × 2 analysis of variance). At day 1, FMD was not significantly increased (P = .329). By day 15, tomato supplementation resulted in an increase in FMD</p>	RCT

				by $3.3\% \pm 1.4\%$ , whereas at the control arm, FMD declined by $-0.5\% \pm 0.6\%$ ( $P = .03$ ); magnitudes of change are absolute FMD values. Total oxidative status decreased at the end of the supplementation period compared with baseline values ( $P = .038$ ). Daily tomato paste consumption exerts a beneficial midterm but not short-term effect on endothelial function. Further studies are warranted to explore the effects of tomato paste on endothelial dilation in different age groups and comorbidities.	
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 <math>39 \pm 6</math> years old; BMI: <math>24.5 \pm 3.3</math> kg/m<sup>2</sup>) 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 (<math>-9.27 \pm 16.8\%</math> ; <math>p &lt; 0.05</math>). Moreover, total plasma antioxidant capacity tended to increase with the high-lycopene tomato sauce, while it decreased slightly with commercial tomato sauce consumption (<math>2.69 \pm 13.4</math> vs <math>-0.05 \pm 0.4</math>; <math>p = 0.058</math>). 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</p> <p>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 inflammation	DiSilvestro RA	<p>Lycopene Concentrate Supplementation Decreases Plasma Values for C-Reactive Protein and oxidized LDL.</p> <p>DiSilvestro RA, Joseph E, DiSilvestro D.</p> <p>The FASEB Journal. 2013;27:638.13</p>	2013	<p>Various lines of indirect evidence suggest that lycopene can exert anti-inflammatory effects relevant to problems such as cardiovascular disease (CVD). However, a beneficial influence for lycopene supplementation on measures relevant to inflammation remain largely lacking. In the present study, a lycopene rich extract from tomato (20 mg lycopene/day in Lyc-O-Mato® tomato lycopene complex), or placebo, was given to healthy middle aged men for 6 weeks (N = 10 per group). Subjects did not have to follow a low lycopene diet, but a preliminary screening eliminated people with a history of frequent tomato product intake. In the lycopene group,</p>	RCT

				<p>plasma c-reactive protein concentrations, which rise with CVD-relevant inflammation, showed a mean decrease of almost 30% (<math>p &lt; 0.05</math>, 2-tailed paired t-test). Placebo gave no statistically significant effect. Lycopene also produced a mean decrease of 5.1% in plasma oxidized LDL values, an atherosclerosis-related measure that can be increased by inflammation (<math>p &lt; 0.05</math>, 2-tailed paired t-test). Although this percent decrease was not tremendously large, longer intervention periods and/or combination with other natural products may heighten the effect. Again, placebo was ineffective. Neither of the lycopene effects was boosted by adding supplementation with zinc arginate (15 mg zinc/day) + selenium (200 <math>\mu</math>g selenium/day) in another group of subjects. These mineral supplements did improve zinc and selenium functional status based on two measures for each mineral. In summary, in a small study, supplementation with a tomato extract-lycopene by itself produced changes in two cardiovascular disease-relevant measures related to inflammation</p>	
CVD:inflammation	Ghavipour M	<p>Tomato juice consumption reduces systemic inflammation in overweight and obese females.</p> <p>Ghavipour M, Saedisomeolia A, Djalali M, Sotoudeh G, Eshraghyan MR, Moghadam AM, Wood LG.</p> <p>Br J Nutr. 2013 Jun;109(11):2031-5. doi:10.1017/S0007114512004278. Epub 2012 Oct 15.</p>	2013	<p>Tomatoes are the richest source of lycopene, a potent antioxidant. Tomato products improve antioxidant defences and reduce the risk of inflammatory diseases, at least partly, due to the presence of lycopene. Lycopene, as an anti-inflammatory agent, prevents the production of inflammatory cytokines. Obesity is a chronic inflammatory condition in which the increased level of body fat leads to an increase in circulating inflammatory mediators. We hypothesised that the consumption of a lycopene-rich food would reduce inflammation in people who are overweight or obese. A total of 106 overweight or obese female students of the Tehran University of Medical Sciences were enrolled and randomly allocated to an intervention group (n 53) or a control group (n 53) consuming 330 ml/d of tomato juice or water, respectively, for 20 d. At baseline and day 20, serum concentrations of IL-6, IL-8, high-sensitivity C-reactive protein and TNF-<math>\alpha</math> were analysed by ELISA and compared between the groups. Serum concentrations of IL-8 and TNF-<math>\alpha</math> decreased significantly in the intervention group compared with the control group and with baseline. Subgroup analysis indicated that this effect was confined to subjects who were overweight. Among obese subjects, serum IL-6 concentration was decreased in the intervention group compared with the control group, with no differences in IL-8 and TNF-<math>\alpha</math> observed. Tomato juice reduces inflammation in overweight and obese females. Thus, increasing tomato intake may provide a useful approach for</p>	RCT

				reducing the risk of inflammatory diseases such as CVD and diabetes, which are associated with obesity.	
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 (&lt;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&amp;3) by rapid ultracentrifugation. Compliance was monitored by assessing lycopene concentration in serum and HDL(2&amp;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&amp;3) following both lycopene interventions (P&lt;.001, for all), while SAA decreased in serum following the lycopene supplement and in HDL(3) following both lycopene interventions (P&lt;.05 for all). PON-1 activity increased in serum and HDL(2&amp;3) in both lycopene groups (P&lt;.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&lt;.05 for all). These results demonstrate that in moderately overweight, middle-aged subjects, increasing lycopene intake leads to changes to HDL(2&amp;3), which we suggest enhanced their antiatherogenic properties. Overall, these results show the heart-protective properties of increased lycopene intake.</p>	RCT
CVD: endothelial function	Gajendragadkar PR	<p>Effects of oral lycopene supplementation on vascular function in patients with cardiovascular disease and healthy volunteers: a randomised controlled trial.</p>	2014	<p>AIMS: The mechanisms by which a 'Mediterranean diet' reduces cardiovascular disease (CVD) burden remain poorly understood. Lycopene is a potent antioxidant found in such diets with evidence suggesting beneficial effects. We wished to investigate the effects of lycopene on the vasculature in CVD patients and separately, in healthy volunteers (HV). METHODS AND</p>	RCT

		<p>Gajendragadkar PR, Hubsch A, Mäki-Petäjä KM, SergM, Wilkinson IB, Cheriyan J.</p> <p>PLoS One. 2014 Jun 9;9(6):e99070. doi:10.1371/journal.pone.0099070. eCollection 2014.</p>		<p>RESULTS: We randomised 36 statin treated CVD patients and 36 healthy volunteers in a 2:1 treatment allocation ratio to either 7 mg lycopene or placebo daily for 2 months in a double-blind trial. Forearm responses to intra-arterial infusions of acetylcholine (endothelium-dependent vasodilatation; EDV), sodium nitroprusside (endothelium-independent vasodilatation; EIDV), and NG-monomethyl-L-arginine (basal nitric oxide (NO) synthase activity) were measured using venous plethysmography. A range of vascular and biochemical secondary endpoints were also explored. EDV in CVD patients post-lycopene improved by 53% (95% CI: +9% to +93% , P=0.03 vs. placebo) without changes to EIDV, or basal NO responses. HVs did not show changes in EDV after lycopene treatment. blood pressure, arterial stiffness, lipids and hsCRP levels were unchanged for lycopene vs. placebo treatment groups in the CVD arm as well as the HV arm. At baseline, CVD patients had impaired EDV compared with HV (30% lower; 95% CI: -45% to -10% , P=0.008), despite lower LDL cholesterol (1.2 mmol/L lower, 95% CI: -1.6 to -0.9 mmol/L, P&lt;0.001). Post-therapy EDV responses for lycopene-treated CVD patients were similar to HVs at baseline (2% lower, 95% CI: -30% to +30% , P=0.85), also suggesting lycopene improved endothelial function.</p> <p>CONCLUSIONS: Lycopene supplementation improves endothelial function in CVD patients on optimal secondary prevention, but not in HVs. ClinicalTrials.gov NCT01100385</p>	
CVD: IMT	Zou ZY	<p>Effects of lutein and lycopene on carotid intima-media thickness in Chinese subjects with subclinical atherosclerosis: a randomised, double-blind, placebo- controlled trial.</p> <p>Zou ZY, Xu XR, Lin XM, Zhang HB, Xiao X, Ouyang L, Huang YM, Wang X, Liu YQ.</p> <p>Br J Nutr. 2014 Feb;111(3):474-80. doi:10.1017/S0007114513002730. Epub 2013 Sep 19.</p>	2014	<p>The aim of the present study was to evaluate the effects of lutein and lycopene supplementation on carotid artery intima-media thickness (CAIMT) in subjects with subclinical atherosclerosis. A total of 144 subjects aged 45-68 years were recruited from local communities. All the subjects were randomly assigned to receive 20 mg lutein/d (n 48), 20 mg lutein/d+20 mg lycopene/d (n 48) or placebo (n 48) for 12 months. CAIMT was measured using Doppler ultrasonography at baseline and after 12 months, and serum lutein and lycopene concentrations were determined using HPLC. Serum lutein concentrations increased significantly from 0.34 to 1.96 µmol/l in the lutein group (P&lt; 0.001) and from 0.35 to 1.66 µmol/l in the combination group (P&lt; 0.001). Similarly, serum lycopene concentrations increased significantly from 0.18 to 0.71 µmol/l in the combination group at month 12 (P&lt; 0.001), whereas no significant change was observed in the placebo group. The mean values of CAIMT decreased significantly by 0.035 mm (P= 0.042) and 0.073 mm (P&lt; 0.001) in the lutein and combination groups at month 12, respectively. The</p>	RCT

			<p>change in CAIMT was inversely associated with the increase in serum lutein concentrations (<math>P &lt; 0.05</math>) in both the active treatment groups and with that in serum lycopene concentrations (<math>\beta = -0.342</math>, <math>P = 0.031</math>) in the combination group. Lutein and lycopene supplementation significantly increased the serum concentrations of lutein and lycopene with a decrease in CAIMT being associated with both concentrations. In addition, the combination of lutein and lycopene supplementation was more effective than lutein alone for protection against the development of CAIMT in Chinese subjects with subclinical atherosclerosis, and further studies are needed to confirm whether synergistic effects of lutein and lycopene exist.</p>	
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