Summary of Research
Oxidative Stress/Damage

Disease: Endpoints of Interest	First Author	Study Title and Complete Citation	Date	Abstract	Study Type
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. Lipids. 1998 Oct;33(10):981-4.	1998	Increase in low density lipoprotein (LDL) oxidation is hypothesized to be causally associated with increasing risk of atherosclerosis and coronary heart disease. In recent epidemiological studies, tissue and serum levels of lycopene, a carotenoid available from tomatoes, have been found to be inversely related to risk of coronary heart disease. A study was undertaken to investigate the effect of dietary supplementation of lycopene on LDL oxidation in 19 healthy human subjects. Dietary lycopene was provided using tomato juice, spaghetti sauce, and tomato oleoresin for a period of 1 wk each. Blood samples were collected at the end of each treatment. Serum lycopene was extracted and measured by high-performance liquid chromatography using an absorbance detector. Serum LDL was isolated by precipitation with buffered heparin, and thiobarbituric acid-reactive substances (TBARS) and conjugated dienes (CD) were measured to estimate LDL oxidation. Both methods, to measure LDL oxidation LDL-TBARS and LDL-CD, were in good agreement with each other. Dietary supplementation of lycopene significantly increased serum lycopene levels by at	Interv

				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 and their possible role in the prevention of cancer. Rao AV, Agarwal S. Nutr Cancer. 1998;31(3):199-203.	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 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.	Interv

CVD: oxidation	Rao AV	Effect of diet and smoking on serum lycopene and lipid peroxidation. Rao AV, Agarwal S. Nutr Res, 1998;18:713–21.	1998	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 *in vivo* antioxidant properties of lycopene.	Interv
CVD: oxidation	Steinberg FM	Antioxidant vitamin supplementation and lipid peroxidation in smokers. Steinberg FM, Chait A. Am J Clin Nutr. 1999 Jun;69(6):1292.	1998	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 IU, 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 peroxyl 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 peroxyl 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.	RCT
CVD: oxidation	Dugas TR	Dietary supplementation with beta-carotene, but not with lycopene, inhibits endothelial cell-mediated oxidation of low-density lipoprot ein.	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 (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	Interv

		Dugas TR, Morel DW, Harrison EH. Free Radic Biol Med.1999 May;26(9-10):1238-44		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. Am J Clin Nutr. 1999 Apr;69(4):712-8.	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 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. 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	RCT

				tomato-free diet (P < 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 < 0.05) and by 42% (95% CI: 5.1% , 78% ; P < 0.05) in the 2 groups of subjects after consumption of the tomato diet. CONCLUSION: The consumption of tomato products may reduce the susceptibility of lymphocyte DNA to oxidative damage	
CVD: oxidation	Sutherland WH	Supplementation with tomato juice increases plasma lycopene but does not alter susceptibility to oxidation of low-density lipoproteins from renal transplant recipients. Sutherland WH, Walker RJ, De Jong SA, Upritchard JE. Clin Nephrol. 1999 Jul;52(1):30-6	1999	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 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). CONCLUSION: In conclusion, these data suggest that increased oxidative stress and susceptibility of LDL to oxidation may not be reduced by increasing plasma lycopene levels with regular consumption of tomato juice in renal transplant recipients.	Interv
CVD: oxidation	Bub A	Moderate intervention with carotenoid-rich vegetable products reduces lipid peroxidation in men. Bub A, Watzl B, Abrahamse L, Delincee H, Adam S, Wever J, Muller H, Rechkemmer G. J Nutr. 2000 Sep;130(9):2200-6.	2000	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	Interv

				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: < 0.05) and lipoprotein oxidizability in terms of an increased lag time (18% , P: < 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.	
CVD: oxidation	Carroll YL	Lipoprotein carotenoid profiles and the susceptibility of low density lipoprotein to oxidative modification in healthy elderly volunteers. Carroll YL, Corridan BM, Morrissey PA. Eur J Clin Nutr. 2000 Jun;54(6):500-7.	2000	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 aged > or =65 y. DESIGN: Randomized placebo controlled double blind study. SETTING: Free living urban adults in Ireland. Subjects: Fifty-one volunteers aged > 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. 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. 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.	RCT

CVD: oxidation	Chopra M	Influence of increased fruit and vegetable intake on plasma and lipoprotein carotenoids and LDL oxidation in smokers and nonsmokers. Chopra M, O'Neill ME, Keogh N, Wortley G, Southon S, Thurnham DI. Clin Chem. 2000 Nov;46(11):1818-29.	2000	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. 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. RESULTS: Baseline concentrations (mean +/- SD) of plasma beta-carotene (0.203+/-0.28 micromol/L vs. 0.412+/-0.34 micromol/L; P <0.005) and lutein (0.180 +/-0.10 vs. 0.242+/-0.11 micromol/L; P<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+/- 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<0.01) compared with depletion. CONCLUSIONS: In this short-term intervention study, a dietary intake of >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.	Interv
CVD: oxidation	Fuhrman B	Lycopene synergistically inhibits LDL oxidation in combination with vitamin E, glabridin, rosmarinic acid, carnosic acid, or garlic. Fuhrman B, Volkova N, Rosenblat M, Aviram M. Antioxid Redox Signal. 2000 Fall;2(3):491-506.	2000	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	Interv

				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-to-cotrienol. 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 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 ($p < 0.01$) 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.	
CVD: oxidation	Porrini M	Lymphocyte lycopene concentration and DNA protection from oxidative damage is increased in women after a short period of tomato consumption. Porrini M, Riso P. J Nutr. 2000 Feb;130(2):189-92.	2000	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 ($P <0.001$) and lymphocyte ($P<0.005$) lycopene concentration and reduced lymphocyte DNA damage by approximately 50% ($P<0.0001$). Beta-carotene concentration increased in plasma ($P<0.05$) but not in lymphocytes after tomato puree consumption. An inverse relationship was found between plasma lycopene concentration ($r = -0.82$, $P<0.0001$) and lymphocyte lycopene concentration ($r = -0.62$, $P<0.01$) 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.	Interv

CVD: oxidation inflammation endothelial function markers	Upritchard JE	Effect of supplementation with tomato juice, vitamin E, and vitamin C on LDL oxidation and products of inf lammatory activity in type 2 diabetes. Upritchard JE, Sutherland WH, Mann JI. Diabetes Care. 2000 Jun;23(6):733-8.	2000	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 METHODS: There were 57 patients with well-controlled type 2 diabetes aged <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. 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. 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.	RCT
CVD: oxidation	Hininger IA	No significant effects of lutein, lycopene or beta- carotene supplementation on biological markers of oxidative stress and LDL oxidizability in healthy adult subjects. Hininger IA, Meyer-Wenger A, Moser U, Wright A, Southon S, Thurnham D, Chopra M, Van	2001	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. 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 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)	RCT

		Den Berg H, Olmedilla B, Favier AE, Roussel AM. J Am Coll Nutr. 2001 Jun;20(3):232-8.		concentrations, protein SH groups. erythrocyte antioxidant enzyme activities (Cu-Zn SOD, Se-GSH-Px) and susceptibility of LDL to copper-induced oxidation. 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. 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.	
CVD: oxidation	Maruyama C	Effects of tomato juice consumption on plasma and lipoprotein carotenoid concentrations and the susceptibility of low density lipoprotein to oxidative modification. Maruyama C, Imamura K, Oshima S, Suzukawa M, Egami S, Tonomoto M, Baba N, Harada M, Ayaori M, Inakuma T, Ishikawa T. J Nutr Sci Vitaminol (Tokyo). 2001 Jun;47(3):213-21	2001	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 ($p<0.01$). In the High group, the lycopene concentration increased 270% each in the VLDL+IDL and LDL fractions, and 330% in the HDL fraction ($p<0.01$). 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 propagationrate 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 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.	RCT
CVD: oxidation BP	John JH	Effects of fruit and vegetable consumption on plasma antioxidant concentrations	2002	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,	RCT

		and blood pressure: a randomised controlled trial. John JH, Ziebland S, Yudkin P, Roe LS, Neil HA; Oxford Fruit and Vegetable Study Group. Lancet. 2002 Jun 8;359(9322):1969-74.		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. 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. 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<0.0001). Systolic blood pressure fell more in the intervention group than in controls (difference=4.0 mm Hg, 2.0-6.0; p<0.0001), as did diastolic blood pressure (1.5 mm Hg, 0.2-2.7; p=0.02). 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.	
CVD: oxidation	Olmedilla B	A European multicentre, placebo-controlled supplementation study with alpha-tocopherol, carotene-rich palm oil, lutein or lycopene: analysis of serum responses. Olmedilla B, Granado F, Southon S, Wright AJ, Blanco I, Gil-Martinez E, van den Berg H, Thurnham D, Corridan B, Chopra M, Hininger I.	2002	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	RCT

		Clin Sci (Lond). 2002 Apr;102(4):447-56.		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.	
CVD: oxidation	Porrini M	Spinach and tomato consumption increases lymphocyte DNA resistance to oxidative stress but this is not related to cell carotenoid concentrations. Porrini M, Riso P, Oriani G. Eur J Nutr. 2002 Jun;41(3):95-100.	2002	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. AIM OF THE STUDY: We evaluated the effect of spinach and spinach+tomato puree consumption on cell DNA resistance to an oxidative stress. METHODS: To this aim, in a dietary controlled intervention study, 9 healthy female volunteers consumed a basal diet low in carotenoids (< 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 H2O2. RESULTS: During the first period of spinach consumption, lymphocyte lutein concentration did not increase significantly (1.6 to 2.2 mmol/1012 cells) while lycopene and beta-carotene concentrations decreased significantly (1.0 to 0.1 mmol/1012 cells, P < 0.001, and 2.2 to 1.2 mmol/1012 cells, P < 0.05, respectively). Lutein and lycopene concentrations increased after spinach+tomato puree consumption (1.2 to 3.5 mmol/1012 cells, P < 0.01, and 0.1 to 0.7 mmol/1012 cells, P < 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 H2O2 insult increased significantly after both the enriched diets (P < 0.01); however, no "additive effect" was seen after spinach + tomato puree consumption. In the spinach + tomato intervention period an inverse correlation was	Interv

				observed between lymphocyte lycopene concentration and DNA damage, but this seems not able to explain the protection observed. CONCLUSIONS: 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.	
CVD: oxidation lipids	Ahuja KD	Effects of two lipid-lowering, carotenoid-controlled diets on the oxidative modification of low-density lipoproteins in free-living humans. Ahuja KD, Ashton EL, Ball MJ. Clin Sci (Lond). 2003 Sep;105(3):355-61.	2003	This study compares the effects of two lipid-lowering diets [a diet enriched in MUFAs (monounsaturated fatty acids) and a HCLF (high-carbohydrate/low-fat) diet] with a controlled carotenoid content on risk factors for coronary heart disease, including in vitro copper-induced LDL (low-density lipoprotein) oxidation and serum lipid levels. A randomized crossover dietary intervention study, with two diets each consumed for 14-16 days, was conducted in 18 women and 13 men aged 20-70 years, recruited via personal contacts and advertisements in newspapers. Both diets (MUFA-enriched diet and HCLF diet) contained the same basic foods and had a controlled carotenoid content, high in lycopene. The in vitro copper-induced oxidation of isolated LDL showed a longer lag phase (mean difference 7.4 min in women and 7.34 min in men) after the MUFA-enriched diet compared with the HCLF diet. Serum total cholesterol, LDL cholesterol and carotenoid levels were similar after the two diets. Serum triacylglycerol levels were significantly lower and those of HDL (high-density lipoprotein) cholesterol were significantly higher at the end of the MUFA-enriched diet 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.	Interv
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. 2003 Mar;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)	Interv

				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) 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	OBJECTIVE: To determine whether dietary supplementation with a natural carotenoid mixture counteracts the enhancement of oxidative stress induced by consumption of fish oil. DESIGN: A randomised double-blind crossover dietary intervention. SETTING: Hugh Sinclair Unit of Human Nutrition, School of Food Biosciences, The University of Reading, Whiteknights PO 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. 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.	RCT

CVD: oxidation	Visioli F	Protective activity of tomato products on in vivo markers of lipid oxidation. Visioli F, Riso P, Grande S, Galli C, Porrini M. Eur J Nutr. 2003 Aug;42(4):201-6.	2003	BACKGROUND: It has been suggested that regular consumption of tomato products improves antioxidant defenses due to their endogenous antioxid ant compounds, notably lycopene. AIM OF THE STUDY: We evaluated the effects of tomato consumption on parameters of lipid oxidation in healthy human volunteers. 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. RESULTS: Carotenoid concentrations decreased significantly during the carotenoid-poor diet ($P < 0.05$), while lycopene concentrations increased significantly after tomato consumption ($P < 0.001$). 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 ($P < 0.001$). This parameter was significantly correlated with lycopene concentration ($r = 0.36$, $P < 0.05$). The excretion of 8-iso-PGF(2alpha) in urine was also significantly lower (-53% , $P < 0.05$ compared with T0) after tomato supplementation. CONCLUSIONS: These results further support a role for tomato products in the prevention of lipid peroxidation, a risk factor of atherosclerosis and cardiovascular disease.	Interv
CVD: oxidation	Briviba K	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. Briviba K, Kulling SE, Moseneder J, Watzl B, Rechkemmer G, Bub A.	2004	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 ($P = 0.44$) 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	RCT

		Carcinogenesis. 2004 Dec;25(12):2373-8. Epub 2004 Aug 12.		approximately 32 (non-smokers) and 39% (smokers). However, this effect was not statistically significant in either group (P = 0.09 for non-smokers and P = 0.12 for smokers). Analysis of the distribution pattern of DNA strand breaks showed a statistically significant (P < 0.05) 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 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 plasma (FRAP). Data were analyzed using Proc Mixed	RCT

				Procedure and associations between antioxidant and lipid measures were identified by Pearson's product moment correlation analysis. 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. 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.	
CVD: oxidation	Rao AV	Processed tomato products as a source of dietary lycopene: bioavailability and antioxidant properties. Rao AV. Can J Diet Pract Res. 2004 Winter;65(4):161-5.	2004	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 ($p < 0.05$), from 181.79 +/- 31.25 to 684.7 +/- 113.91 nmol/L. Similarly, total antioxidant potential increased significantly ($p < 0.05$), from 2.26 +/- 0.015 to 2.38 +/- 0.17 mmol/L Trolox equivalent. Lipid and protein oxidation was reduced significantly ($p < 0.05$). The results suggest that a tomato-rich diet containing different sources of lycopene can increase serum lycopene levels and reduce oxidative stress effectively.	Interv
CVD: oxidation	Riso P	Lycopene and vitamin C concentrations increase in plasma and lymphocytes after tomato intake. Effects on cellular antioxidant protection. Riso P, Visioli F, Erba D, Testolin G, Porrini M.	2004	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. 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	Interv

		Eur J Clin Nutr. 2004 Oct;58(10):1350-8.		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). RESULTS: Dietary intervention with tomato products increased lycopene concentration both in plasma (P < 0.001) and lymphocytes (P < 0.01). Vitamin C concentrations increased by approximately 35% in plasma (P < 0.05) and by approximately 230% in lymphocytes (P < 0.005). Vitamin E decreased significantly in plasma (P < 0.0001) but not in lymphocytes. Finally, there was an improved protection from DNA oxidative damage (P < 0.05) with no significant effect on MDA levels. 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.	
CVD: oxidation	Tyssandier V	Effect of tomato product consumption on the plasma status of antioxidant microconstituents and on the plasma total antioxidant capacity in healthy subjects. Tyssandier V, Feillet-Coudray C, Caris-Veyrat C, Guilland JC, Coudray C, Bureau S, Reich M, Amiot- Carlin MJ, Bouteloup-Demange C, Boirie Y, Borel P. J Am Coll Nutr. 2004 Apr;23(2):148-56.	2004	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. DESIGN: Medium-term dietary supplementation study. SETTING: Human Nutrition Laboratory, Clermont-Ferrand, France. SUBJECTS: Twenty healthy young (20 < years < 40), non obese (18 < BMI (kg/m2) < 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 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.	Interv

				RESULTS: Supplementation with tomato puree significantly increased plasma lycopene, beta-carotene and lutein. Conversely it did not significantly affect plasma vitamin 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 ($p < 0.05$) 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 ($p < 0.05$) to the status of lycopene, vitamin C and beta-carotene. 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.	
CVD: oxidation	Bub A	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. Bub A, Barth SW, Watzl B, Briviba K, Rechkemmer G. Br J Nutr. 2005 Mar;93(3):291-7.	2005	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 ($P<0.05$) 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 ($P<0.05$) 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 PON1-192 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.	RCT
CVD: oxidation	Porrini M	Daily intake of a formulated tomato drink affects carotenoid plasma and lymphocyte concentrations	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	RCT

		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.		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.	
CVD: oxidation lipids	Ahuja KD	Effects of olive oil and tomato lycopene combination on serum lycopene, lipid profile, and lipid oxidation. Ahuja KD, Pittaway JK, Ball MJ. Nutrition. 2006 Mar;22(3):259-65. Epub 2006 Jan 18.	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. METHODS: This was a randomized crossover dietary intervention study carried out in Launceston, Tasmania, Australia in healthy free-living individuals. Twenty-one healthy subjects who were 22 to 70 y old were recruited by advertisements in newspapers and a university newsletter. A randomized dietary intervention was done with two diets of 10 d each. One diet was high in olive oil and the other was high in carbohydrate and low in olive oil; the two diets contained the same basic foods and a controlled carotenoid content high in lycopene. RESULTS: Significant increases (P<0.001) in serum lycopene concentration on both diets were to similar final concentrations. Higher serum high-density lipoprotein cholesterol (P<0.01), lower ratio of total cholesterol to high-density lipoprotein (P<0.01), and lower triacylglycerols (P<0.05) occurred after the olive oil diet compared with the high-carbohydrate, low-fat diet. There was no difference in total antioxidant status and susceptibility of serum lipids to oxidation. CONCLUSIONS: 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	Interv

				the risk of coronary heart disease by improving the serum lipid profile compared with a high-carbohydrate, low-fat, lycopene-rich diet.	
CVD: oxidation Lipids HgA1c	Bose KS	Effect of long term supplementation of tomatoes (cooked) on levels of antioxidant enzymes, lipid peroxidation rate, lipid profile and glycated haemoglobin in Type 2 diabetes mellitus. Bose KS, Agrawal BK. West Indian Med J. 2006 Sep;55(4):274-8.	2006	The objective of the present study is to evaluate the beneficial effect of tomatoes, which are a rich source of lycopene, a relatively new carotenoid known to play an important role in human health. In this study, the lipid peroxidation rate was investigated by estimating malondialdehyde (TBARS) levels of antioxidant enzymes like SOD, GSH-Px, GR, GSH, lipid profile, which includes total cholesterol, triglycerides, high density lipoprotein, low density lipoprotein, very low density lipoprotein,and glycated haemoglobin HbA1c in (n = 40) the Type 2 diabetic group (n = 40) and an age-matched control group (n = 50). Significantly lower levels of antioxidant enzymes and very high lipid peroxidation rate in the Type 2 diabetic group were observed when compared to controls ($p < 0.001$). Likewise, significantly higher levels of lipid profile and glycated haemoglobin (HbA1c) in the diabetic group were observed when compared with control ($p < 0.001$). Long term tomato supplementation in diabetes mellitus showed a significant improvement in the levels of antioxidant enzymes and decreased lipid peroxidation rate ($p < 0.001$), but there were no significant changes in lipid profile and glycated haemoglobin HbA1c levels ($p > 0.10$). These findings suggest that tomato lycopene may have considerable therapeutic potential as an antioxidant but there was no significant lipid lowering effect in Type 2 diabetes mellitus.	Interv
CVD: oxidation lipids BP	Engelhard YN	Natural antioxidants from tomato extract reduce blood pressure in patients with grade-1 hypertension: a double-blind, placebo-controlled pilot study. Engelhard YN, Gazer B, Paran E. Am Heart J. 2006 Jan;151(1):100.	2006	BACKGROUND: Treatment of hypertension (HT) can reduce the risk for cardiovascular diseases. Tomato extract contains carotenoids such as lycopene, beta carotene, and vitamin E, which are known as effective antioxidants, to inactivate free radicals, and to slow the progression of atherosclerosis. The purpose of our study was to evaluate the effect of tomato extract on systolic and diastolic blood pressure in grade-1 HT, on serum lipoproteins, plasma homocysteine, and oxidative stress markers. METHODS: This study is a single-blind, placebo-controlled trial. Thirty-one subject with grade-1 HT, without concomitant diseases, who required no antihypertensive or lipid-lowering drug therapy, who were recruited from primary care clinic, completed the trial. Subjects entered a 4-week placebo period, then an 8-week treatment period with tomato extract, 250 mg Lyc-O-Mato, and a 4-week control period with placebo. RESULTS: Systolic blood pressure decreased from 144 (SE +/- 1.1) to 134 mm Hg (SE +/- 2, $P < .001$), and diastolic blood pressure decreased from 87.4 (SE +/- 1.2) to 83.4 mm Hg (SE +/- 1.2, $P < .05$). No changes in blood pressure were demonstrated during placebo periods. Thiobarbituric acid-reactive substances, a lipid peroxidation products marker, decreased	RCT

				from 4.58 (SE +/- 0.27) to 3.81 nmol/mg (SE +/- 0.32, P < .05). No significant changes were found in lipid parameters. 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.	
CVD: oxidation lipids	Madrid AE	[Short-term Lycopersicum esculentum consumption may increase plasma high density lipoproteins and decrease oxidative stress]. [Article in Spanish] Madrid A E, Vásquez Z D, Leyton A F, Mandiola C, Escobar F JA. Rev Med Chil. 2006 Jul;134(7):855-62. Epub 2006 Aug 29.	2006	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 METHODS: Seventeen healthy volunteers were studied. They received a supplement of pure tomato juice during 7 days. At baseline, at the end of the supplementarion 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-enzimatic antioxidants (lycopene and a-tocopherol) and plasma lipoproteins. RESULTS: Lycopene level increased early and significantly in comparison with basal levels (48% ; p < 0.05). TRAP, catalase and superoxide dismutase did not change significantly. HDL cholesterol increased significantly in 5.6+/-4.3 mg/dL (p < 0.002) on the second sampling period, improving the ratio cholesterol/HDL. It returned to baseline in the third period. 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.	Interv
CVD: oxidation lipids	Misra R	LycoRed as an alternative to hormone replacement therapy in lowering serum lipids and oxidative stress markers: a randomized controlled clinical trial.	2006	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.	RCT

		Misra R1, Mangi S, Joshi S, Mittal S, Gupta SK, Pandey RM. J Obstet Gynaecol Res. 2006 Jun;32(3):299-304.		METHODS: Forty-one healthy postmenopausal women were randomly allocated to receive either continuous combined HRT (n = 21) or LycoRed (n = 20) for six months. Serum lipid profile, marker of lipid peroxidation (malondialdehyde), and the level of endogenous antioxidant (glutathione) were measured at the baseline, and 3 and 6 months after the intervention in both groups. RESULTS: At 6 months, HRT resulted in a significant decrease in total cholesterol (TC) level by 23.5% , low-density lipoproteins (LDL) by 19.6% , and an increase in high-density lipoproteins (HDL) by 38.9% . The LycoRed group showed similar changes in TC (-24.2%), LDL (-14.9%) and HDL (+26.1%). Triglyceride levels showed a smaller though significant increase at 6 months, but not at 3 months, in both groups. There was no significant change in the very LDL (VLDL) level in either group. Malondialdehyde levels decreased significantly by 16.3% and 13.3% , whereas glutathione levels increased significantly by 5.9% and 12.5% in HRT and LycoRed groups, respectively. CONCLUSION: Both HRT and LycoRed had a favorable effect on serum lipids and oxidative stress markers which were comparable. LycoRed can be used as an alternative to HRT to reduce the risk of atherosclerosis in postmenopausal women.	
CVD: oxidation	Paterson E	Supplementation with fruit and vegetable soups and beverages increases plasma carotenoid concentrations but does not alter markers of oxidative stress or cardiovascular risk factors. Paterson E, Gordon MH, Niwat C, George TW, Parr L, Waroonphan S, Lovegrove JA. J Nutr. 2006 Nov;136(11):2849-55.	2006	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%) ($P < 0.01$) and decreased the plasma homocysteine concentration by 8.8% ($P < 0.01$). 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.	RCT

CVD: oxidation inflammation	Riso P	Effect of a tomato-based drink on markers of inflammation, immunomodulation, and oxidative stress. Riso P, Visioli F, Grande S, Guarnieri S, Gardana C, Simonetti P, Porrini M. J Agric Food Chem. 2006 Apr 5;54(7):2563-6.	2006	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 immunoessay), on basal lymphocyte DNA damage (by comet assay), and on F2-isoprostane excretion (by LC-MS/MS), were investigated in 26 healthy young volunteers. 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.	RCT
CVD: oxidation inflammation	Sanchez-Moreno C	Mediterranean vegetable soup consumption increases plasma vitamin C and decreases F2-isoprostanes, prostaglandin E2 and monocyte chemot actic protein-1 in healthy humans. Sanchez-Moreno C, Cano MP, de Ancos B, Plaza L, Olmedilla B, Granado F, Martin A. J Nutr Biochem. 2006 Mar;17(3):183-9. Epub 2005 Aug 15.	2006	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 men and 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 < .05) in plasma vitamin C occurred 4 h postdose in both men and women. Vitamin C concentrations were significantly higher (P < .03) on Days 7 and 14 of the intervention. Baseline concentrations of uric acid and 8-epi-PGF2alpha were significantly higher (P < or = .032) in men than in women. Baseline concentrations of 8-epi-PGF2alpha decreased significantly (P < or = .05) by Day 14 of the intervention. A significant inverse correlation was observed between vitamin C and 8-epi-PGF2alpha (r = -.415, P = .049). Baseline concentrations of PGF2 and MCP-1 were significantly higher (P< or = .025) in men than in women but decreased significantly (P< or = .05) 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	Interv

				increases plasma concentrations of vitamin C and significantly decreases 8-epi-PGF2alpha, PGE2 and MCP-1 concentrations in healthy humans.	
CVD: oxidation	Zhao X	Modification of lymphocyte DNA damage by carotenoid supplementation in postmenopausal women. Zhao X, Aldini G, Johnson EJ, Rasmussen H, Kraemer K, Woolf H, Musaeus N, Krinsky NI, Russell RM, Yeum KJ. Am J Clin Nutr. 2006 Jan;83(1):163-9.	2006	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. OBJECTIVE: Our aim was to determine the protective effect of carotenoids against DNA damage. 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 onsume 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. RESULTS: At day 57, all carotenoid-supplemented groups showed significantly lower endogenous DNA damage than at baseline ($P < 0.01$), whereas the placebo group did not show any significant change. Significantly less ($P < 0.05$) endogenous DNA damage was found as early as day 15 in the mixed carotenoid ($P < 0.01$) and beta-carotene ($P < 0.05$) groups. 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 achieved by diet, or a larger dose (12 mg) of individual carotenoids exerts protection against DNA damage.	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.	2007	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. 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	Interv

		Singapore Med J. 2007 May;48(5):415-20.		lipoprotein and very low density lipoprotein in a coronary heart disease (CHD) group and an age-matched control group. RESULTS: We observed significantly lower levels of serum antioxidant enzymes and very high lipid peroxidation rate in the CHD group, when compared to the controls (p-value is less than 0.001). At the same time, we observed significantly higher levels of lipids in the CHD group, when compared to the controls (p-value is less than 0.001). 60 days of tomato supplementation in the CHD group showed a significant improvement in the levels of serum enzymes involved in antioxidant activities and decreased lipid peroxidation rate (p-value is less than 0.001), but there were no significant changes in lipid profile (p-value is greater than 0.10). 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.	
CVD: oxidation	Neyestani TR	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. Neyestani TR, Shariatzadeh N, Gharavi A, Kalayi A, Khalaji N. J Endocrinol Invest. 2007 Nov;30(10):833-8.	2007	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 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. 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<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. CONCLUSIONS: Lycopene, probably by increasing TAC and inhibiting MDA-LDL formation, may attenuate T cell-dependent adaptive (pro-atherogenic) immune response. Meanwhile,	RCT

				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 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.	RCT
CVD: oxidation	Briviba K	No differences in DNA damage and antioxidant capacity between intervention groups of	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	RCT

		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.		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.	
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. Vasc Health Risk Manag. 2008;4(1):213-22.	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 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.	Interv
CVD: oxidation	Devaraj S	A dose-response study on the effects of purified lycopene supplementation on biomarkers of oxidative stress.	2008	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.	RCT

		Devaraj S, Mathur S, Basu A, Aung HH, Vasu VT, Meyers S, Jialal I. J Am Coll Nutr. 2008 Apr;27(2):267-73.		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 & hydroxynonenals (MDA & HNE), urinary F(2)-isoprostanes}, and markers of DNA damage in urine and lymphocytes. Healthy adults (n = 77, age > or = 40 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. RESULTS: Independent of the dose, plasma lycopene levels significantly increased in all lycopene supplemented groups versus placebo ($p < 0.05$). ANOVA revealed a significant decrease in DNA damage by the comet assay ($p = 0.007$), and a significant decrease in urinary 8-hydroxy deoxoguanosine (8-OHdG) at 8 weeks versus baseline ($p = 0.0002$), 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. CONCLUSIONS: Thus, purified lycopene was bioavailable and was shown to decrease DNA oxidative damage and urinary 8-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 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.	RCT
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/m2) were compared with a control group of eight lean, age and gender-matched subjects (BMI 21.6 +/- 0.6 kg/m2),	Interv

				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 IL-6 and conjugated dienes correlated inversely with carotenoids (P < 0.05). 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) (P < 0.001) occurred in the treatment vs. the placebo group, respectively. Markers of inflammation and oxidation products were not altered by lycopene. 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.	
CVD: oxidation lipids	Talvas J	Differential effects of lycopene consumed in tomato paste and lycopene in the form of a purified extract on target genes of cancer prostatic cells. Talvas J, Caris-Veyrat C, Guy L, Rambeau M, Lyan B, Minet-Quinard R, Lobaccaro JM, Vasson MP, Georgé S, Mazur A, Rock E. Am J Clin Nutr. 2010 Jun;91(6):1716-24. Epub 2010 Apr 14	2010	BACKGROUND: Prospective studies indicate that tomato consumers are protected against prostate cancer. Lycopene has been hypothesized to be responsible for tomato health benefits. OBJECTIVE: Our aim was to differentiate the effects of tomato matrix from those of lycopene by using lycopene-rich red tomatoes, lycopene-free yellow tomatoes, and purified lycopene. DESIGN: Thirty healthy men (aged 50-70 y old) were randomly assigned to 2 groups after a 2-wk washout period. In a crossover design, each group consumed yellow and red tomato paste (200 g/d, which provided 0 and 16 mg lycopene, respectively) as part of their regular diet for 1 wk separated by 2 wk of washout. Then, in a parallel design, the first group 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. 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	RCT

				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. CONCLUSION: Dietary lycopene can affect gene expression whether or not it is included in its food matrix. This trial was registered by the French Health Ministry at http://www.sante-sports.gouv.fr as 2006-A00396-45.	
CVD: oxidation lipids	Barona J	A Mediterranean-style low-glycemic-load diet increases plasma carotenoids and decreases LDL oxidation in women with metabolic syndrome. Barona J, Jones JJ, Kopec RE, Comperatore M, Andersen C, Schwartz SJ, Lerman RH, Fernandez ML. J Nutr Biochem. 2011 Jul 18. [Epub ahead of print]	2011	Thirty-five women with metabolic syndrome and high plasma low-density lipoprotein (LDL) cholesterol (≥100 mg/dl) participated in a dietary intervention consisting of a Mediterranean-style low-glycemic-load diet for 12 weeks. Participants were randomly allocated to consume diet only (n=15) or diet plus a medical food containing soy protein and plant sterols (n=20). Plasma concentrations of carotenoids, lipoprotein subfractions and oxidized LDL (OxLDL) were measured. Independent of treatment, women had a significant increase in plasma lutein (P<.0001) and β-carotene (P<.0001), while plasma lycopene was reduced (P<.05) after 12 weeks. Low-density lipoprotein cholesterol was reduced from 138±35 to 114±33 mg/dl (P<.0001). In addition, decreases were observed in the atherogenic subfractions: large very low-density lipoprotein (P<.05), small LDL (P<.00001) and medium high-density lipoprotein (P<.05). oxidized LDL was significantly reduced by 12% in both groups (P<.01). Changes in OxLDL were inversely correlated with plasma lutein (r=-.478, P<.0001). The data indicate that women complied with the dietary regimen by increasing fruits and vegetable intake. Decreased consumption of high-glycemic foods frequently co-consumed with lycopene-rich tomato sauce such as pasta and pizza may be responsible for the lowering of this carotenoid in plasma after 12 weeks. These results also suggest that plasma lutein concentrations may protect against oxidative stress by reducing the concentrations of OxLDL.	Interv
CVD: oxidation lipids endothelial function BP	Kim JY	Effects of lycopene supplementation on oxidative stress and markers of endothelial function in healthy men. Kim JY, Paik JK, Kim OY, Park HW, Lee JH, Jang Y, Lee JH.	2011	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. 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. RESULTS: Serum lycopene increased in a dose-dependent manner after 8-week supplementation (P<0.001). The 15 mg/day group had greater increase in plasma SOD activity (P=0.014) and reduction in lymphocyte DNA comet tail length (P=0.042) than the	RCT

		Atherosclerosis. 2011 Mar;215(1):189-95. Epub 2010 Dec 9.		placebo group. Intragroup comparison revealed a 23% increase in RH-PAT index from baseline (1.45±0.09 vs. 1.79±0.12; P=0.032) in the 15 mg/day group after 8-week. hs-CRP, systolic blood pressure, sICAM-1 and sVCAM-1 significantly decreased, and β-carotene and LDL-particle size significantly increased only in the 15 mg/day group. Interestingly, the beneficial effect of lycopene supplementation on endothelial function (i.e., RH-PAT and sVCAM-1) were remarkable in subjects with relatively impaired endothelial cell function at initial level. Changes in RH-PAT index correlated with SOD activity (r=0.234, P=0.017) especially in the 15 mg lycopene/day group (r=0.485, P=0.003), lymphocyte DNA comet tail moment (r=-0.318, P=0.001), and hs-CRP (r=-0.238, P=0.011). In addition, changes in lycopene correlated with hs-CRP (r=-0.230, P=0.016) and SOD activity (r=0.205, P=0.037). CONCLUSION: An increase in serum lycopene after supplementation can reduce oxidative stress which may play a role in endothelial function	
CVD: oxidation	Martínez-Tomás R	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. Martínez-Tomás R, Larqué E, González-Silvera D, Sánchez-Campillo M, Burgos MI, Wellner A, Parra S, Bialek L, Alminger M, Pérez-Llamas F. Eur J Nutr. 2011 Jun 7. [Epub ahead of print]	2011	AIM: To evaluate the effect of the daily intake of a fruit & vegetable soup with high in vitro bioaccessibility of carotenoids on β-carotene and lycopene serum concentrations. METHODS: Fourteen healthy young men (24 ± 1 years) received 300 mL/day of a carrot, tomato, and broccoli soup, containing 3.9 mg β-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. RESULTS: The in vitro bioaccessibility of β-carotene and lycopene was 55 and 43% , respectively, in the soup. Serum β-carotene concentrations were significantly higher than baseline (0.33 ± 0.05 μmol/L) after 3 weeks (0.69 ± 0.06 μmol/L) and 4 weeks (0.78 ± 0.10 μmol/L) of soup consumption (P < 0.001). Serum lycopene was also significantly higher compared with baseline levels (0.26 ± 0.08-0.56 ± 0.04 μmol/L and 0.60 ± 0.04 μmol/L, after 3 and 4 weeks, respectively) (P < 0.001). 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 β-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. 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 longer than that of β-carotene, which may be important for studies evaluating both carotenoids.	Interv

CVD: oxidation lipids inflammation endothelial function	Burton-Freeman B	Protective activity of processed tomato products on postprandial oxidation and inflammation: a clinical trial in healthy weight men and women. Burton-Freeman B, Talbot J, Park E, Krishnankutty S, Edirisinghe I. Mol Nutr Food Res. 2012 Apr;56(4):622-31. doi: 10.1002/mnfr.201100649. Epub 2012 Feb 14.	2012	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 RESULTS: Twelve women and 13 men (mean age = 27 ± 8 years; mean body mass index= 22 ± 2) consumed high-fat meals known to induce postprandial oxidative stress on two separate occasions containing either processed tomato product or non-tomato alternative. Blood samples were collected at 0, 30, 60, 90, 120 min, then hourly until 360 min. Flow-mediated dilation (FMD) was performed at 0 and 210 min. Endpoints included changes in glucose, insulin, lipids, oxidized low-density lipoprotein (OxLDL), inflammatory cytokines, and FMD. Both meals induced increases in plasma glucose, insulin, and lipid concentrations ($p < 0.05$). A trend for higher triglycerides at >240 min was observed after the tomato meal ($p = 0.006$). Tomato significantly attenuated high-fat meal-induced LDL oxidation ($p < 0.05$) and rise in interleukin-6 ($p < 0.0001$), a proinflammatory cytokine and inflammation marker. 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.	RCT
CVD: oxidation endothelial function	Xanplanteris P	Tomato paste supplementation improves endothelial dynamics and reduces plasma total oxidative status in healthy subjects. Xaplanteris P, Vlachopoulos C, Pietri P, Terentes- Printzios D, Kardara D, Alexopoulos N, Aznaouridis K, Miliou A, Stefanadis C. Nutr Res. 2012 May;32(5):390-4. doi:10.1016/j.nutres.2012.03.011. Epub 2012 May 15.	2012	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 by 3.3% ± 1.4% , whereas at the control arm, FMD declined by -0.5% ± 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	RCT

				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	A regular lycopene enriched tomato sauce consumption influences antioxidant status of healthy young-subjects: A crossover study Abete I, Perez-Cornago A, Navas-Carretero S, Bondia-Pons I, Zulet MA, Martinez, JA Journal of Functional Foods Volume 5, Issue 1, January 2013, Pages 28–35	2013	Tomato and tomato products are known as potential factors to decrease oxidative stress biomarkers. Therefore, the objective was to evaluate the effects of consumption of two tomato sauces with different concentrations of lycopene on oxidative stress markers. Thirty healthy subjects (Men/women: 9/21; Aged 39 ± 6 years old; BMI: 24.5 ± 3.3 kg/m2) were recruited to participate in a double-blind crossover study. Participants had to consume 160 g/day of tomato sauce, while maintaining their usual dietary and physical activity habits. The regular consumption of the high-lycopene tomato sauce induced a significant reduction in the oxidized-LDL cholesterol levels (−9.27 ± 16.8% ; $p < 0.05$). Moreover, total plasma antioxidant capacity tended to increase with the high-lycopene tomato sauce, while it decreased slightly with commercial tomato sauce consumption (2.69 ± 13.4 vs −0.05 ± 0.4; $p = 0.058$). Lipid, glucose profile and C-reactive protein concentrations were stable during both intervention periods, as well as anthropometric and body composition variables. Thus, the daily consumption of 160 g of a high-lycopene tomato sauce improved oxidized-LDL cholesterol levels, evidencing the putative role of lycopene in combination with other bioactive compounds in the prevention of oxidative stress related diseases	RCT
CVD: oxidation inflammation	DiSilvestro RA	Lycopene Concentrate Supplementation Decreases Plasma Values for C-Reactive Protein and oxidized LDL DiSilvestro RA, Joseph E, DiSilvestro D. The FASEB Journal. 2013;27:638.13	2013	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, plasma c-reactive protein concentrations, which rise with CVD-relevant inflammation, showed a mean decrease of almost 30% ($p < 0.05$, 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 ($p < 0.05$, 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 µg 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	RCT

CVD: oxidation lipids inflammation	McEneny J	Lycopene intervention reduces inflammation and improves HDL functionality in moderately overweight middle-aged individuals. McEneny J, Wade L, Young IS, Masson L, Duthie G, McGinty A, McMaster C, Thies F. J Nutr Biochem. 2013 Jan;24(1):163-8. doi: 10.1016/j.jnutbio.2012.03.015. Epub 2012 Jul 21.	2013	The management of overweight subjects by interventions aimed at reducing inflammation is highly desirable. To date, observational studies have identified a link between increased dietary antioxidant intake and reduced cardiovascular morbidity. However, direct trial evidence regarding the ability of antioxidants to influence inflammation is lacking. Therefore, this study examined lycopene's ability to lower systemic and high-density lipoprotein (HDL)-associated inflammation in moderately overweight middle-aged subjects. Serum was collected before and after a 12-week intervention from 54 moderately overweight, middle-aged individuals. Subjects were randomised to one of three groups: control diet (<10 mg lycopene/week), lycopene-rich diet (224-350 mg lycopene/week) and lycopene supplement (70 mg lycopene/week). HDL was subfractionated into HDL(2&3) by rapid ultracentrifugation. Compliance was monitored by assessing lycopene concentration in serum and HDL(2&3). Systemic and HDL-associated inflammation was assessed by measuring serum amyloid A (SAA) levels. HDL functionality was determined by monitoring the activities of paraoxonase-1 (PON-1), cholesteryl ester transfer protein (CETP) and lecithin cholesterol acyltransferase (LCAT). Lycopene increased in serum and HDL(2&3) following both lycopene interventions (P<.001, for all), while SAA decreased in serum following the lycopene supplement and in HDL(3) following both lycopene interventions (P<.05 for all). PON-1 activity increased in serum and HDL(2&3) in both lycopene groups (P<.05, for all). Furthermore, the activity of CETP decreased in serum following the lycopene supplement, while the activity of LCAT increased in serum and HDL(3) following both lycopene interventions (P<.05 for all). These results demonstrate that in moderately overweight, middle-aged subjects, increasing lycopene intake leads to changes to HDL(2&3), which we suggest enhanced their antiatherogenic properties. Overall, these results show the heart-protective properties of increased lycopene intake.	RCT