CARDIOVASCULAR DISEASE (CVD)
Lycopene Supplementation and Disease Risk

Disease type	First Author	Study Title and Complete Citation	Date	Abstract	Study Type	G.Tom +, N, -	P.Tom +, N, -	F.Tom +, N, -	Lyco +, N, -	Other +, N, -
Heart: 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 from 4.58 (SE +/- 0.27) to 3.81 nmol/mg (SE +/- 0.32, P < .05). No significant changes were found in lipid parameters.	RCT				(-)	BP TBARS Pre-htn

				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.						
Heart: BP	Paran E	The effects of natural antioxidants from tomato extract in treated but uncontrolled hypertensive patients. Paran E, Novack V, Engelhard YN, Hazan-Halevy I. Cardiovasc Drugs Ther. 2009 Apr;23(2):145-51. Epub 2008 Dec 4	2009	PURPOSE: To evaluate the effect of adding tomato extract to the treatment regime of moderate hypertensives with uncontrolled blood pressure (BP) levels. METHODS: Fifty four subjects with moderate HT treated with one or two antihypertensive drugs were recruited and 50 entered two double blind cross-over treatment periods of 6 weeks each, with standardized tomato extract or identical placebo. Plasma concentrations of lycopene, nitrite and nitrate were measured and correlated with BP changes. RESULTS: There was a significant reduction of systolic BP after 6 weeks of tomato extract supplementation, from 145.8 +/- 8.7 to 132.2 +/- 8.6 mmHg ($p < 0.001$) and 140.4 +/- 13.3 to 128.7 +/- 10.4 mmHg ($p < 0.001$) in the two groups accordingly. Similarly, there was a decline in diastolic BP from 82.1 +/- 7.2 to 77.9 +/- 6.8 mmHg ($p = 0.001$) and from 80.1 +/- 7.9 to 74.2 +/- 8.5 mmHg ($p = 0.001$). There was no significant change in systolic and diastolic BP during the placebo period. Serum lycopene level increased from 0.11 +/- 0.09 at baseline, to 0.30 +/- 01.3 micromol/L after tomato extract therapy ($p < 0.001$). There was a significant correlation between systolic BP and lycopene levels ($r = -0.49$, $p < 0.001$). CONCLUSIONS: Tomato extract when added to patients treated with low doses of ACE inhibition, calcium channel blockers or their combination with low dose diuretics, had a clinically significant effect-reduction of BP by	RCT				(-) BP	Tom extract unctrl Htn w/meds

				more than 10 mmHg systolic and more than 5 mmHg diastolic pressure. No side-effects to treatment were recorded and the compliance with treatment was high. The significant correlation between systolic blood pressure values and level of lycopene suggest the possibility of cause-effect relationships.						
Heart: BP	Ried K	Dark chocolate or tomato extract for prehypertension: a randomised controlled trial. Ried K, Frank OR, Stocks NP. BMC Complement Altern Med. 2009 Jul 8;9:22	2009	BACKGROUND: Flavanol-rich chocolate and lycopene-rich tomato extract have attracted interest as potential alternative treatment options for hypertension, a known risk factor for cardiovascular morbidity and mortality. Treatment of prehypertension (SBP 120-139/DBP 80-89 mmHg) may forestall progression to hypertension. However, there has been only limited research into non-pharmacological treatment options for prehypertension. We investigated the effect of dark chocolate or tomato extract on blood pressure, and their acceptability as an ongoing treatment option in a prehypertensive population. METHODS: Our trial consisted of two phases: a randomised controlled three-group-parallel trial over 12 weeks (phase 1) followed by a crossover of the two active treatment arms over an additional 12-week period (phase 2). Group 1 received a 50 g daily dose of dark chocolate with 70% cocoa containing 750 mg polyphenols, group 2 were allocated one tomato extract capsule containing 15 mg lycopene per day, and group 3 received one placebo capsule daily over 8 weeks followed by a 4-week washout period. In phase 2 the active treatment groups were crossed over to receive the alternative treatment. Median blood pressure, weight, and abdominal circumference were measured 4-weekly, and other characteristics including physical activity, general health, energy, mood, and acceptability of treatment were assessed by questionnaire at 0, 8 and 20 weeks. We analysed changes over time using a linear	RCT				N	Tom extract BP

				mixed model, and one time point differences using Kruskal-Wallis, Fisher's-Exact, or t-tests. RESULTS: Thirty-six prehypertensive healthy adult volunteers completed the 6-month trial. Blood pressure changes over time within groups and between groups were not significant and independent of treatment. Weight and other characteristics did not change significantly during the trial. However, a marked difference in acceptability between the two treatment forms (chocolate or capsule) was revealed ($p < 0.0001$). Half of the participants allocated to the chocolate treatment found it hard to eat 50 g of dark chocolate every day and 20% considered it an unacceptable long-term treatment option, whereas all participants found it easy and acceptable to take a capsule each day for blood pressure. CONCLUSION: Our study did not find a blood pressure lowering effect of dark chocolate or tomato extract in a prehypertensive population. Practicability of chocolate as a long-term treatment option may be limited.						
Heart: BP, oxidation and endothelial function	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. Atherosclerosis. 2011 Mar;215(1):189-95. Epub 2010 Dec 9.	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 placebo group. Intragroup comparison revealed a 23% increase in RH-PAT index from	RCT				N BP Endothelial function Oxidative stress CRP	

				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						
Heart: lipids	Fuhrman B	Hypocholesterolemic effect of lycopene and beta-carotene is related to suppression of cholesterol synthesis and augmentation of LDL receptor activity in macrophages. Fuhrman B, Elis A, Aviram M. Biochem Biophys Res Commun. 1997 Apr 28;233(3):658-62.	1997	Beta-Carotene and lycopene are derived from plants, and they share similar initial synthetic pathway with cholesterol, which is synthesized in animal but not in plant cells. Thus, we sought to analyze the effect of carotenoids on macrophage cholesterol metabolism, in comparison to the effect of LDL cholesterol and of the cholesterol synthesis inhibitor, fluvastatin. In J-774 A. 1 macrophage cell line, the cellular cholesterol synthesis from [3H]-acetate, but not from [14C] mevalonate, was suppressed by 63% any by 73% following cell incubation with beta-carotene or lycopene (10 microM) respectively, in comparison to a 90% and 91% inhibition by LDL (100 micrograms of cholesterol), or by fluvastatin (10 micrograms/ml) respectively. However, unlike LDL derived cholesterol, which also suppresses macrophage LDL receptor activity, lycopene and beta-carotene augmented the activity of the macrophage LDL receptor, similarly to the effect of fluvasfatin. In agreement with these in vitro	Interv				(-)	↓ LDL

				observations, dietary supplementation of tomato's lycopene (60 mg/day) to 6 males for a 3 months period resulted in a significant 14% reduction in their plasma LDL cholesterol concentrations. We thus conclude that dietary supplementation of carotenoids may act as moderate hypocholesterolemic agents, secondary to their inhibitory effect on macrophage 3-hydroxy-3-methyl glutaryl coenzyme A (HMGCoA) reductase, the rate limiting enzyme in cholesterol synthesis.						
Heart: lipids	Böhm V	Intestinal absorption of lycopene from different matrices and interactions to other carotenoids, the lipid status, and the antioxidant capacity of human plasma. Böhm V, Bitsch R. Eur J Nutr. 1999 Jun;38(3):118-25.	1999	BACKGROUND: The bioavailability of carotenoids has been investigated in animal studies as well as in human studies, so far mostly for beta-carotene. Only few results exist for lycopene. In recent studies, lycopene was significantly better available from processed tomatoes compared to raw tomatoes, when using daily intakes between 16.5 mg and 75 mg lycopene. AIM OF THE STUDY: In a comparative study the availability of a low oral lycopene dosage of 5 mg/d from different food matrices versus soft gel capsules containing tomato oleoresin was assessed. In addition to the plasma carotenoid content, the effect of lycopene ingestion on other plasma carotenoids, the lipid status parameters, and the antioxidant activity was estimated. METHODS: Twenty-two female adults (20-27 y) were randomized in three groups and were advised to minimize their carotenoid intake for two weeks. After this initial period, two groups received a portion of tomatoes or tomato juice adjusted to a lycopene dose of 5 mg/d, the third group ingested the same dose comprised in soft gel capsules containing tomato oleoresin. During the test period of 6 weeks, the participants continued reducing the intake of carotenoids from food. Fasting blood samples were withdrawn prior to the study, before supplementation started, and then weekly while supplemented. Seven-day dietary records were prepared before the study started and after one week of	RCT		N Lipids and Ox status		N Lipids and Ox status	

				supplementation. Carotenoids were analyzed by reversed phase HPLC with diode array detection. Dietary records were evaluated using the computer software EBIS 2.1. The plasma total cholesterol, HDL cholesterol, and triglycerides were determined enzymatically. In addition, the antioxidant activity of plasma was estimated by using the TEAC and the TRAP assays. RESULTS: The basal levels of lycopene in plasma were comparable for all groups (0.2-0.3 mumol/l) and decreased significantly during the two weeks of depletion to approximately 50% of the basal values. Other plasma carotenoids such as beta-carotene and beta-cryptoxanthin decreased significantly, too, whereas lutein and zeaxanthin remained unchanged. After supplementation with tomato oleoresin capsules or tomato juice, the plasma lycopene increased significantly, while it remained unchanged during intake of tomatoes. Normal dietary habits were practised of all volunteers before and during the study except vitamin C whose intake was significantly lower during the study period, because the probands were recommended to reduce the intake of fruits and vegetables. Lycopene supplementation did not affect the lipid status parameters of the three groups. After ingestion of lycopene the antioxidant activity of the plasma was not altered. Mean TEAC values were estimated to 0.33 +/- 0.05 mmol/l and TRAP values to 1.0 +/- 0.1 mmol/l and showed no significant differences in all groups during the whole study period. CONCLUSIONS: The bioavailability of lycopene varied significantly depending on the administered matrix. Lycopene from tomato oleoresin capsules and tomato juice (processed tomatoes) was better absorbed from the intestine than lycopene from raw tomatoes. The daily intake of 5 mg lycopene, an intake comparable to the usual daily carotenoid intake, did not affect cholesterol						

				and triglycerides in plasma or its antioxidant capacity.						
Heart: lipids and oxidation	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),	RCT				(-) TG	

				but total cholesterol, HDL and LDL levels were not significantly changed by the consumption of the carotenoid mixture.						
Heart: lipids and oxidation	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 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	RCT		N Lipids Ox status PSA IGF-1		N Lipids Ox status PSA IGF-1	

				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.						
Heart: oxidation and 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), 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	Interv				N Ox Inflam (-) ↓ with ↑ BMI	Plasma lyco ↓ with ↑ BMI

				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.						
Heart: oxidation	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	Interv		N Lipids ~~~~~ (-) Oxidation		N Lipids ~~~~~ (-) Oxidation	Tomato juice, spaghetti sauce, tomato oleoresin extract LDL ox TBARS Healthy

				lycopene significantly increased serum lycopene levels by at least twofold. Although there was no change in serum cholesterol levels (total, LDL, or high-density lipoprotein), serum lipid peroxidation and LDL oxidation were significantly decreased. These results may have relevance for decreasing the risk for coronary heart disease.						
Heart: 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		(-)/N		(-)/N	TBARS Protein thiols 8-odg Lipid prot DNA ox Healthy

Heart: oxidation	Steinberg FM	Antioxidant vitamin supplementation and lipid peroxidation in smokers. Steinberg FM, Chait A. Am J Clin Nutr. 1999 Jun;69(6):1292.	1999	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		(-)/N			LDL ox Smokers
Heart: oxidation	Carroll YL	Lipoprotein carotenoid profiles and the susceptibility of low density lipoprotein to oxidative modification in healthy elderly volunteers. Carroll YL, Corridan	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	RCT				(-) Lipids ~~~~~ N Oxidation	LDLox

		BM, Morrissey PA. Eur J Clin Nutr. 2000 Jun;54(6):500-7.		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.						
Heart: oxidation	Fuhrman B	Lycopene synergistically inhibits LDL oxidation in combination with vitamin E, glabridin, rosmarinic acid, carnosic acid, or garlic. Fuhrman B, Volkova	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	In vitro/ Inv n=4				(-) in vitro ~~~~~ (-) in vivo	LDL ox Healthy

		N, Rosenblat M, Aviram M. Antioxid Redox Signal. 2000 Fall;2(3):491-506.		tomato oleoresin (lipid extract of tomatoes containing 6% lycopene, 0.1% beta-carotene, 1% vitamin E, and polyphenols), after which it was oxidized by the addition of 5 micromol/liter of CuSO4. Tomato oleoresin exhibited superior capacity to inhibit LDL oxidation in comparison to pure lycopene, by up to five-fold [97% vs. 22% inhibition of thiobarbituric acid reactive substances (TBARS) formation, and 93% vs. 27% inhibition of lipid peroxides formation, respectively]. Because tomato oleoresin also contains, in addition to lycopene, vitamin E, flavonoids, and phenolics, a possible cooperative interaction between lycopene and such natural antioxidants was studied. A combination of lycopene (5 micromol/liter) with vitamin E (alpha-tocopherol) in the concentration range of 1-10 micromol/liter resulted in an inhibition of copper ion-induced LDL oxidation that was significantly greater than the expected additive individual inhibitions. The synergistic antioxidative effect of lycopene with vitamin E was not shared by gamma-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.						
Heart: 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 Den Berg H, Olmedilla B, Favier AE, Roussel AM. J Am Coll Nutr. 2001 Jun;20(3):232-8.	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) 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.	RCT				N LDLox	Ox stress Anti-Ox enzyme ativity LDL ox Healthy

				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.						
Heart: 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. Clin Sci (Lond). 2002 Apr;102(4):447-56.	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 were not present in the supplement), whereas lycopene supplementation (from tomato	RCT				N	Ox stress Healthy

				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 did oxidative stress assessment revealing no remarkable findings.						
Heart: 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. Carcinogenesis. 2004 Dec;25(12):2373-8. Epub 2004 Aug 12.	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	RCT				(-)/N	Ox stress DNA Immune function Smokers/ non-smokers

				increases in total plasma lycopene and resulted in decreased levels of DNA strand breaks of approximately 32 (non-smokers) and 39% (smokers). However, this effect was not statistically significant in either group (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).						
Heart: oxidation	Porrini M	Daily intake of a formulated tomato drink affects carotenoid plasma and lymphocyte concentrations and improves cellular antioxidant protection. Porrini M, Riso P, Brusamolino A, Berti C, Guarnieri S, Visioli F. Br J Nutr. 2005 Jan;93(1):93-9.	2005	The salutary characteristics of the tomato are normally related to its content of carotenoids, especially lycopene, and other antioxidants. Our purpose was to verify whether the daily intake of a beverage prototype called Lyc-o-Mato((R)) containing a natural tomato extract (Lyc-o-Mato((R)) oleoresin 6 %) was able to modify plasma and lymphocyte carotenoid concentrations, particularly those of lycopene, phytoene, phytofluene and beta-carotene, and to evaluate whether this intake was sufficient to improve protection against DNA damage in lymphocytes. In a double-blind, cross-over study, twenty-six healthy subjects consumed 250 ml of the drink daily, providing about 6 mg lycopene, 4 mg phytoene, 3 mg phytofluene, 1 mg beta-carotene and 1.8 mg alpha-tocopherol, or a placebo drink. Treatments were separated by a wash-out period. Plasma and lymphocyte carotenoid and alpha-tocopherol concentrations were determined by HPLC, and DNA damage by the comet assay. After 26 d of consumption of the drink, plasma carotenoid levels increased significantly: concentrations of lycopene were	RCT				(-)	Ox

				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.						
Heart: oxidation	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,	RCT				N/(-)	TNFa DNA damage F2 isoprost Healthy

				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.						
Heart: 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	RCT				(-)	DNA ox Comet assay Healthy

				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.						
Heart: oxidation	Devaraj S	A dose-response study on the effects of purified lycopene supplementation on biomarkers of oxidative stress. Devaraj S, Mathur S, Basu A, Aung HH, Vasu VT, Meyers S, Jialal I. J Am Coll Nutr. 2008 Apr;27(2):267-73.	2008	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. 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.	RCT				(-)	(-) DNA comet (-) IsoPros

				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.						
Heart: oxidation and inflammation	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,	Interv				N CRP MDA Adhesion molecules	

				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.						
Heart: platelet	O'Kennedy N	Effects of antiplatelet components of tomato extract on platelet function in vitro and ex vivo: a time-course cannulation study in healthy humans. O'Kennedy N, Crosbie L, van Lieshout M, Broom JI, Webb DJ, Duttaroy AK. Am J Clin Nutr. 2006 Sep;84(3):570-9.	2006	BACKGROUND: Natural antithrombotic agents that influence platelet function are of potential interest for primary prevention of cardiovascular disease. Previous reports showed that tomato extracts inhibit platelet aggregation in vitro, but little is known of the active components, their mode of action, or their efficacy in vivo. OBJECTIVE: The objectives of the study were to examine the antiplatelet activity of specific tomato components by in vitro experimentation and to establish their ex vivo efficacy in healthy humans. DESIGN: The mechanisms of action of antiplatelet components isolated from tomato extracts were examined in vitro. A 7-h time-course study was carried out in cannulated human subjects (n = 23) to determine the ex vivo efficacy of a supplement drink containing tomato extract and the onset and duration of antiplatelet effects. RESULTS: The inhibition of ADP-, collagen-, thrombin-, and arachidonate-mediated platelet aggregation by tomato extract components appears to be linked to the inhibition of glycoprotein IIb/IIIa and platelet secretory mechanisms. We found a significant	Interv			(-)		FTE

				inhibition of baseline platelet function, from 2.9 +/- 1.4% (optimal ADP concentrations; P = 0.03) to 20.0 +/- 4.9% (suboptimal ADP concentrations; P < 0.001), 3 h after supplementation with a dose of tomato extract equivalent to 6 tomatoes. The observed effects persisted for >12 h. Coagulation variables were not affected. CONCLUSIONS: The ingestion of tomato components with in vitro antiplatelet activity significantly affects ex vivo platelet function. The reported cardioprotective effects of tomatoes are potentially linked to a modulation of platelet function.						
Heart: platelet	O'Kennedy N	Effects of tomato extract on platelet function: a double-blinded crossover study in healthy humans. O'Kennedy N, Crosbie L, Whelan S, Luther V, Horgan G, Broom JI, Webb DJ, Duttaroy AK. Am J Clin Nutr. 2006 Sep;84(3):561-9.	2006	BACKGROUND: Aqueous extracts from tomatoes display a range of antiplatelet activities in vitro. We previously showed that the active components also alter ex vivo platelet function in persons with a high response to ADP agonist. OBJECTIVE: The objective was to evaluate the suitability of a tomato extract for use as a dietary supplement to prevent platelet activation. DESIGN: A randomized, double-blinded, placebo-controlled crossover study was conducted in 90 healthy human subjects selected for normal platelet function. Changes from baseline hemostatic function were measured 3 h after consumption of extract-enriched or control supplements. RESULTS: Significant reductions in ex vivo platelet aggregation induced by ADP and collagen were observed 3 h after supplementation with doses of tomato extract equivalent to 6 (6TE) and 2 (2TE) tomatoes [3 micromol ADP/L: 6TE (high dose), -21.3%; 2TE (low dose), -12.7%; P < 0.001; 7.5 micromol	RCT			(-)		FTE

				ADP/L: 6TE, -7.8%, 2TE, -7.6%; P < 0.001; 3 mg collagen/L: 6TE, -17.5%; 2TE, -14.6%; P = 0.007]. No significant effects were observed for control supplements. A dose response to tomato extract was found at low levels of platelet stimulation. Inhibition of platelet function was greatest in a subgroup with the highest plasma homocysteine (P < 0.05) and C-reactive protein concentrations (P < 0.001). CONCLUSION: As a functional food or dietary supplement, tomato extract may have a role in primary prevention of cardiovascular disease by reducing platelet activation, which could contribute to a reduction in thrombotic events.						