

## Clinical Studies on Tea Leaf (*Camellia sinensis* [L.] Kuntze)

### Cardiovascular

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Leenen <i>et al.</i> , 2000	Plasma antioxidant activity	C, R, CO n=21 healthy volunteers, 10 male, 11 female	1 day (tests at baseline and several times up to 2 hours post-tea drinking)	300 ml black or green tea	Aqueous infusion of black or green tea. 2 g dried leaf in 300 ml boiled water, with or without milk (brands not stated) vs. water	Consumption of a single dose of black or green tea induced a significant rise in plasma antioxidant activity ( $p < 0.001$ ). Plasma was analyzed for total catechins and antioxidant activity using the ferric-reducing ability of plasma (FRAP) assay. Addition of milk did not interfere with the increase. A larger increase was observed for green tea vs. black tea.
Hodgson <i>et al.</i> , 2000	Lipoprotein oxidation	C, R, Cm n=20 healthy males	90 minutes	400 ml black or green tea/day	Aqueous infusion of black tea or sencha (Japanese green tea). 1.9 g dried leaf in 400 ml boiled water for 4 minutes (brands not stated) vs. water control with matched caffeine content	Significant increases in urinary 4-O-methylgallic acid for black and green tea ( $p < 0.0001$ ) were observed. Caffeine did not significantly influence lipoprotein oxidation. Only black tea had a mild acute effect on <i>ex vivo</i> lipoprotein oxidation in human serum, but effect was short-lived and of borderline significance.
Dulloo <i>et al.</i> , 1999	Energy expenditure and fat oxidation	R, PC n=10 healthy males	24 hours on 3 occasions	Two, 250 mg capsules 3x/day, green tea extract (150 mg caffeine, 375 mg catechins)	Exolise® green tea leaf alcoholic dry extract vs. 150 mg caffeine/day vs. placebo (cellulose)	Compared to placebo, tea extract resulted in a significant increase in 24-hour energy expenditure (4%; $p < 0.01$ ) and significant decrease in 24-hour respiratory quotient (from 0.88 to 0.85; $p < 0.001$ ) with no change in urinary nitrogen. Urinary norepinephrine excretion was higher in tea group than placebo (40%, $p < 0.05$ ). Authors concluded that tea has thermogenic properties and promotes fat oxidation.
Geleijnse <i>et al.</i> , 1999	Aortic atherosclerosis	P n=3,454 men and women, free of cardiovascular disease at baseline	2–3 years after baseline assessment; medium duration of follow-up was 1.9 years	125 ml black tea 3.0–3.5x/day	Aqueous infusion of black tea leaf (brands not stated)	Multivariable analyses showed a significant inverse association of tea intake with severe aortic atherosclerosis. Odds ratios (OR) decreased from 0.54 (95% confidence interval [CI], 0.32–0.92) for drinking 125–250 ml (1–2 cups) of tea per day to 0.31 (CI, 0.16–0.59) for drinking more than 500 ml/day (4 cups per day). Associations were stronger in women than men. Association of tea intake with mild and moderate atherosclerosis was not statistically significant. Authors concluded that drinking tea provides a protective effect against ischemic heart disease. (Often called the Rotterdam Study.)
Hodgson <i>et al.</i> , 1999	Blood pressure	C, R, Cm, CO n=20 healthy males	21 days; 7 days each intervention	400 ml black or green tea 4x/day	Aqueous infusion of black tea or sencha (Japanese green tea). 1.9 g dried leaf in 400 ml boiled water for 4 minutes (brands not stated) vs. water control with matched caffeine content	Black (and not green) tea produced a transient (within the first 30 minutes) increase in blood pressure relative to that produced by caffeine. Consumption over 7 days of either black or green tea had no effect on ambulatory blood pressure.

**KEY:** C – controlled, CC – case-control, CH – cohort, CI – confidence interval, Cm – comparison, CO – crossover, CS – cross-sectional, DB – double-blind, E – epidemiological, LC – longitudinal cohort, MA – meta-analysis, MC – multi-center, n – number of patients, O – open, OB – observational, OL – open label, OR – odds ratio, P – prospective, PB – patient-blind, PC – placebo-controlled, PG – parallel group, PS – pilot study, R – randomized, RC – reference-controlled, RCS – retrospective cross-sectional, RS – retrospective, S – surveillance, SB – single-blind, SC – single-center, U – uncontrolled, UP – unpublished, VC – vehicle-controlled.

## Clinical Studies on Tea Leaf (*Camellia sinensis* [L.] Kuntze) (cont.)

### Cardiovascular (cont.)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Sesso <i>et al.</i> , 1999	Myocardial infarction	MC, CC n=340 case-control pairs, white men and women, no prior history of myocardial infarction or angina pectoris (<76 years)	Home interviews conducted 10 weeks after hospital discharge	0 to ≥ 1 cup/day green tea	Aqueous infusion of black tea leaf (brands not stated) vs. coffee and decaffeinated coffee	Only tea was inversely associated with risk of myocardial infarction. 24.9% of cases and 32.0% of controls drank >1 cup/day. Regular tea drinkers had a significantly lower risk of myocardial infarction compared to non-tea drinkers (OR=0.55, 95% CI, 0.36–0.85), independent of coronary risk factors and lipids. The heaviest tea drinkers had more favorable HDL cholesterol levels.
van het Hof <i>et al.</i> , 1999	Plasma antioxidant activity	CO n=18 healthy adults	3 days	1 cup green tea, black tea, or black tea with milk 8x/day (1 cup every 2 hours)	Aqueous infusion of black tea leaf or green tea leaf (brands not stated) with or without milk vs. water	Catechin levels in blood rapidly increased upon repeated tea consumption. Addition of milk did not affect any parameters measured. Accumulation of catechins in LDL particles was not sufficient to improve intrinsic resistance of LDL to oxidation <i>ex vivo</i> .
Princen <i>et al.</i> , 1998	Plasma antioxidant activity	R, SB, PC n=29 healthy smokers, 13 male, 16 female	1 month	One, 150 ml cup black or green tea 6x/day, or 3.6 g isolated green tea polyphenols/day	Aqueous infusion of black tea leaf or green tea leaf (brands not stated) vs. isolated green tea polyphenols vs. placebo	Authors concluded that black or green tea at 6 cups/day had no effect on plasma lipids and no sparing effect on plasma antioxidant vitamins, and that intake of a high dose of isolated green tea polyphenols decreases plasma vitamin E. No effect was found on LDL cholesterol oxidation <i>ex vivo</i> after consumption of green or black tea or intake of green tea polyphenol isolate.
Ishikawa <i>et al.</i> , 1997	Antioxidant activity; susceptibility of LDL cholesterol to oxidation	R, Cm n=22 normo-lipidemic healthy male volunteers	2 months (4 weeks no tea, 4 weeks tea; control group, 8 weeks water)	150 ml black tea 5x/day	Aqueous infusion of 2.2 g Twinings® Darjeeling black tea leaf vs. water	After 4-week treatment period, lag time before initiation of LDL cholesterol oxidation was significantly (p<0.01) prolonged from 54 to 62 minutes. LDL cholesterol exposed to tea had reduced oxidizability. 1 and 2 hours after tea ingestion, levels of EGCG and ECG in plasma increased significantly (p<0.05). Authors speculated that tea may ameliorate atherosclerosis by suppressing oxidation of LDL cholesterol.
van het Hof <i>et al.</i> , 1997	Antioxidant activity, resistance of LDL cholesterol to oxidation	PG, Cm n=45 healthy non-smoking volunteers	One month (2 weeks mineral water, 2 weeks tea) control group, 4 weeks water	150 ml, 6x/day black tea or green tea prepared from freeze-dried, water-soluble extractive	Aqueous infusions of 0.5 g Lipton® freeze-dried black tea leaf extract and 0.5 g Lipton green tea leaf extract vs. mineral water control	Significant increase in total antioxidant activity of plasma occurred after 4 weeks of green tea, or alter serum lipid concentrations. This tea preparation, dosage and duration of use had no effect on variables of oxidative stress to lipids or serum lipid concentrations or resistance of LDL cholesterol to oxidation <i>ex vivo</i> .
Kono <i>et al.</i> , 1996	Hypocholesterolemia	E, MC n=2,062 Japanese male self-defense officials	2 years (1991–92)	Average 1 cup, 3x/day green tea	Aqueous infusion of green tea leaf (brands not stated)	Green tea consumption was inversely associated with serum levels of total cholesterol (TC), and LDL cholesterol, but not with either high-density lipoprotein (HDL) cholesterol or triglycerides. 10 cups/day of green tea was associated with differences of 6.2 mg/dl in TC (95% CI, 0.4–12.1) and 6.2 mg/dl in LDL cholesterol (95% CI, 0.7–11.7). These findings of association of green tea with blood cholesterol suggest a possible causal relationship.
Imai and Nakachi, 1995	Cardiovascular disease and liver disorders	E, P, CS n=1,371 Japanese men (>40 years)	5 years (1986–90)	≤ 3 cups/day to ≥ 10 cups/day green tea	Aqueous infusion of green tea leaf (brands not stated)	As daily green tea intake increased from less than 3 to 4–9, and more than 10 cups, researchers observed significantly increased serum HDL and decreased LDL lipoprotein levels. Additionally, increased green tea consumption was associated with significantly improved liver profiles in which aspartate aminotransferase and alanine aminotransferase levels dropped. An inverse association between green tea ingestion and various serum markers shows that green tea may act protectively against cardiovascular disease and disorders of the liver.

**KEY:** C – controlled, CC – case-control, CH – cohort, CI – confidence interval, Cm – comparison, CO – crossover, CS – cross-sectional, DB – double-blind, E – epidemiological, LC – longitudinal cohort, MA – meta-analysis, MC – multi-center, n – number of patients, O – open, OB – observational, OL – open label, OR – odds ratio, P – prospective, PB – patient-blind, PC – placebo-controlled, PG – parallel group, PS – pilot study, R – randomized, RC – reference-controlled, RCS – retrospective cross-sectional, RS – retrospective, S – surveillance, SB – single-blind, SC – single-center, U – uncontrolled, UP – unpublished, VC – vehicle-controlled.

## Clinical Studies on Tea Leaf (*Camellia sinensis* [L.] Kuntze) (cont.)

### Cardiovascular (cont.)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Hertog <i>et al.</i> , 1993	Coronary heart disease	P n=805 elderly Dutch men	30 years (1960–1990)	1 cup, 2–4x/day black tea	Aqueous infusion of black tea leaf (brands not stated)	Black tea consumption contributed about 70% to daily flavonoid intake. Authors concluded that flavonoids in regularly consumed foods and beverages, such as black tea, may reduce the risk of death from coronary heart disease in elderly men.
Kono <i>et al.</i> , 1992	Serum lipid concentrations and atherosclerosis	E, CS n=1 306 male Japanese self-defense officials (49–56 years)	27 months (October 1986–December 1988)	0 to ≥ 9 cups/day green tea	Aqueous infusion of green tea leaf (brands not stated)	Increased green tea consumption, especially more than 9 cups/day, is associated with decreased total serum cholesterol and decreased LDL cholesterol, very low density lipoproteins and triglycerides, increased HDL, and reduced atherogenic index. Adjusted mean concentrations of total cholesterol were 8 mg/dl lower in men drinking 9 cups or more/day than those drinking zero to 2 cups/day.
Stensvold <i>et al.</i> , 1992	Coronary heart disease	CS, P n=20,089 Norwegian men and women (9,856 men, 10,233 women without history of cardiovascular disease or diabetes)	12 years (1976–1988)	0 to ≥ 5 cups/day black tea	Aqueous infusion of black tea leaf (brands not stated)	Men and women who drank 5 or more cups of black tea per day had lower cholesterol levels than non-tea drinkers. Tea drinkers were less likely to die from heart attack, and systolic blood pressure was inversely related to tea consumption. The mean serum cholesterol decreased with increasing tea consumption; the linear trend coefficient corresponded to a difference of 0.24 mmol/l (9.3 mg/dl) in men and 0.15 mmol/l (5.8 mg/dl) in women between drinkers of less than 1 cup and those of 5 or more cups/day.

### Cancer

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
August <i>et al.</i> , 1999	Colon cancer	Phase I/II study n=14 normal volunteers	24 hours	0.6, 1.2, or 1.8 green tea solids	Green tea solids dissolved in warm water (brand not stated)	Blood samples taken 2, 4, 8, and 24 hours after tea ingestion. Rectal biopsies at 4, 8, and 24 hours. 71% of subjects responded to green tea with at least a 50% inhibition of prostaglandin E <sub>2</sub> (PGE <sub>2</sub> ) levels at 4 hours, indicating possible chemoprevention of colorectal cancer.
Li <i>et al.</i> , 1999	Oral mucosa leukoplakia	R, DB, PC n=59 oral mucosa leukoplakia patients	6 months	Two, 380 mg mixed tea extract capsules 4x/day, plus topical application of 10% mixed tea in glycerol smeared on mucosa lesion 3x/day	External: 10% mixed tea extract in glycerol vs. placebo and glycerin. Internal: 380 mg capsule of mixed tea extract composed of 66.7% green tea aqueous dry native extract, 16.7% green tea polyphenols, and 16.7% tea pigments (theaflavins, thearubigins, and theabromine)	After 6 months, size of oral lesion decreased in 37.9% of 29 treated patients and increased in 3.4% compared to decrease in 10% of 30 control patients and increase of 6.7%. Incidence of micronucleated exfoliated oral mucosa cells in treatment group was lower than in control group (p<0.01). Significant differences (p<0.05) in number and total volume of silver-stained Nucleolar Organizer Regions (AgNOR) and proliferating index of Proliferation Cell Nuclear Antigen (PCNA) indicating decrease of cell proliferation in treatment group. Overall results provide some direct evidence on protective effects of tea on oral cancer.
Nakachi <i>et al.</i> , 1998	Stage I, II, and III breast cancer	E n=472 patients with Stage I, II, and III breast cancer	7 years	≤ 4 cups/day vs. ≥ 5 cups/day green tea	Aqueous infusion of green tea leaf (brands not stated)	Increased consumption of green tea was correlated with decreased recurrence of Stage I and Stage II breast cancer (p<0.05 for crude disease-free survival). No improvement in prognosis was observed in Stage III breast cancer.

**KEY:** C – controlled, CC – case-control, CH – cohort, CI – confidence interval, Cm – comparison, CO – crossover, CS – cross-sectional, DB – double-blind, E – epidemiological, LC – longitudinal cohort, MA – meta-analysis, MC – multi-center, n – number of patients, O – open, OB – observational, OL – open label, OR – odds ratio, P – prospective, PB – patient-blind, PC – placebo-controlled, PG – parallel group, PS – pilot study, R – randomized, RC – reference-controlled, RCS – retrospective cross-sectional, RS – retrospective, S – surveillance, SB – single-blind, SC – single-center, U – uncontrolled, UP – unpublished, VC – vehicle-controlled.

## Clinical Studies on Tea Leaf (*Camellia sinensis* [L.] Kuntze) (cont.)

### Cancer (cont.)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Hartman et al., 1998	Rectal and colon cancer	E, CH n=27,111 male smokers (50–69 years)	8 years	0 cups/day vs. < 1 cup/day vs. ≥ 1 cup/day green tea	Aqueous infusion of black tea leaf. No standard preparation (brands not stated)	This study does not support the hypothesis that coffee and tea protect against colorectal cancer risk. Tea had little effect on incidence of rectal cancer. A positive association was seen for increased consumption of tea and colon cancer.
Ji et al., 1997	Pancreatic and colorectal cancers	E, CC n=2,266 Chinese patients with newly diagnosed cancers: 931 colon, 884 rectum, 451 pancreas, 1,1552 controls	33 months (October 1990– June 1993)	1–199g/month to ≥ 300g/month green tea leaves	Aqueous infusion of green tea leaf (brands not stated)	Significant inverse association with each cancer was observed with increasing green tea dosage. Women with highest tea consumption had 33% reduced risk of colon cancer, 43% reduced risk of rectal cancer, and 47% reduced risk of pancreatic cancer (p=0.07, 0.001, and 0.008 respectively). For men, 18% reduced risk of colon cancer, 43% reduction risk of rectal cancer, and 47% reduced risk of pancreatic cancer (p=0.38, 0.04 and 0.04, respectively).
Imai et al., 1997	Cancer prevention (type not stated)	P, CH n=8,552 Japanese men and women	10 years	Range extending to > 10 cups/day green tea	Aqueous infusion of green tea leaf (brands not stated)	Green tea consumption delayed onset of cancer incidence, especially in females drinking more than 10 cups/day. Preventive effects were not statistically significant in males. Relative risk of cancer incidence (females RR = 0.57, 95% CI = 0.33–0.98; males RR = 0.68, 95% CI = 0.39–1.21) was lowest among those with highest consumption levels.
Yu et al., 1995	Stomach cancer	CC, MC n=1,422 Chinese patients, 711 matched controls (<80 years)	27 months (October 1991– December 1993)	Varied	Aqueous infusion of green tea leaf (brands not stated)	Protective effect against stomach cancer from green tea (OR=0.71; 95% CI, 0.54–0.93). Adjusted OR decreased as consumption increased (p=0.006).
Ohno et al., 1995	Lung cancer	CC n=999 333 Japanese male and female patients	4 years (1988–1991)	1–4 cups/day to ≥ 10 cups/day green tea	Aqueous infusion of green tea leaf (brands not stated)	Odds ratios in females: 1–4 cups/day 0.77 (0.28–3.13), 5–9 cups/day 0.77 (0.26–2.25), 10 or more cups/day 0.57 (0.31–1.06). Corresponding numbers for males: 0.85 (0.46–1.55), 0.85 (0.46–1.56), 0.57 (0.31–1.06). Risk reduction was detected mainly in squamous cell carcinoma.
Gao et al., 1994	Esophageal cancer	E, RS, CC, MC n=734 Chinese patients, 1,552 controls (30–74 years)	28 months (October 1990– January 1993)	0 to ≥ 200 g /month green tea leaves	Aqueous infusion of green tea leaf (brands not stated)	Protective effect of green tea on esophageal cancer was observed among women (OR=0.50, 95% CI=0.30–0.83). Risk decreased significantly with increased consumption (p=0.05) in women, but not in men.

**KEY:** C – controlled, CC – case-control, CH – cohort, CI – confidence interval, Cm – comparison, CO – crossover, CS – cross-sectional, DB – double-blind, E – epidemiological, LC – longitudinal cohort, MA – meta-analysis, MC – multi-center, n – number of patients, O – open, OB – observational, OL – open label, OR – odds ratio, P – prospective, PB – patient-blind, PC – placebo-controlled, PG – parallel group, PS – pilot study, R – randomized, RC – reference-controlled, RCS – retrospective cross-sectional, RS – retrospective, S – surveillance, SB – single-blind, SC – single-center, U – uncontrolled, UP – unpublished, VC – vehicle-controlled.

## Clinical Studies on Tea Leaf (*Camellia sinensis* [L.] Kuntze) (cont.)

Other						
Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Hegarty <i>et al.</i> , 2000	Osteoporosis	CS n=1,256 post-menopausal women (65–76 years old) tea group n=1,134 non-tea group n=122	1 day (BMD measured and questionnaires filled out)	≥ 1 cup/day black or green tea	Aqueous infusions of green tea leaf and black tea leaf with or without milk (brands not stated)	Compared with non-tea drinkers, tea drinkers had significantly greater (~5%) mean bone mineral density (BMD) measurements, adjusted for age and body mass index, at lumbar spine (0.033 g/cm <sup>2</sup> ; p=0.02). Differences at femoral neck (0.013 g/cm <sup>2</sup> ) were not significant. Authors concluded that nutrients in tea, such as flavonoids, may influence BMD and tea may protect against osteoporosis in older women.
Goto <i>et al.</i> , 1999	Effect on fecal flora	O n=35 residents in long-term care facility fed same diet of rice gruel and minced food	6 weeks	Green tea extract, 3x/day with meals (300 mg total catechins/day)	Green tea leaf extract (brand not stated)	Compared to baseline, all fecal parameters decreased significantly during tea extract administration including moisture content, pH, ammonia, sulfide, and oxidation-reduction potential (ORP). These reductions indicated favorable improvements of subject's bowel conditions.
Goto <i>et al.</i> , 1998	Effect on fecal flora	O n=15 male and female nursing home residents fed by nasogastric or gastric tube	3 weeks	161.3 mg, 3x/day green tea extract (300 mg total catechins/day)	Green tea leaf extract, 62.5% total catechins (30.5% EGCG, 18.5% EGC, 7.0% ECG, 6.5% EC) (brand not stated)	Compared to baseline, lactobacilli and bifidobacteria levels increased significantly (p<0.01–0.05). Levels of enterobacteriaceae, bacteroidaceae, eubacteria, and total bacteria decreased significantly compared to baseline (p<0.01–0.05). Levels of unwanted bacterial metabolites decreased significantly at 21 days (p<0.01–0.05). Fecal pH lowered significantly (p<0.05). After 7 days of discontinuance, all levels returned to pretrial levels.
van het Hof <i>et al.</i> , 1998	Bioavailability of catechins	R, C, CO n=12 healthy male (5) and female (7) adults	3 weeks (crossover at 1-week intervals)	1 single dose (3 g tea solids) green tea, black tea, or black tea with milk	Aqueous infusions of 3 g green tea leaf (900 mg catechins) and 3 g black tea leaf (300 mg catechins), with and without milk	Consumption of green tea or black tea resulted in a rapid increase of catechin levels in blood. Maximum changes were reached after 2.3 hours for green and 2.2 hours for black tea. Addition of milk did not impair tea catechin bioavailability.
Lecomte, 1985	Obesity	R, DB, PC n=60 obese women (30–45 years)	1 month (follow-ups at 15 and 30 days treatment)	Eight, 250 mg capsules/day green tea leaf powder with meals (2 breakfast, 3 lunch, 3 dinner)	Arkocaps/Phytotrim® green tea leaf powder (250 mg powdered leaf per capsule) vs. placebo	Significant average weight loss of 1.7 kg at day 15 and 2.9 kg at day 30 in green tea group. Significant decrease in waist measurement after 30 days. Significant reductions in total cholesterol and blood triglycerides but no reduction in HDL cholesterol. Author concluded that green tea powder caused significant weight loss compared to placebo and demonstrates utility in treatment of obesity.

**KEY:** C – controlled, CC – case-control, CH – cohort, CI – confidence interval, Cm – comparison, CO – crossover, CS – cross-sectional, DB – double-blind, E – epidemiological, LC – longitudinal cohort, MA – meta-analysis, MC – multi-center, n – number of patients, O – open, OB – observational, OL – open label, OR – odds ratio, P – prospective, PB – patient-blind, PC – placebo-controlled, PG – parallel group, PS – pilot study, R – randomized, RC – reference-controlled, RCS – retrospective cross-sectional, RS – retrospective, S – surveillance, SB – single-blind, SC – single-center, U – uncontrolled, UP – unpublished, VC – vehicle-controlled.