Clinical Studies on Garlic (*Allium sativum* L.)

Cardiovascular

Hyperlipidemia/Hypercholesterolemia/Hypertension/Related Risk Factors

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Berthold *et al.*, 1998	Hypercholesterolemia (mean TC 291 mg/dl and mean LDL 207 mg/dl)	R, DB, PG n=25 (diet not controlled)	12 weeks following a 4-week washout period	5 mg, 2x/day or placebo (with meals)	Tegra® garlic oil (oil bound to b-cyclodextrin for slow release)	The garlic preparation did not influence serum lipoproteins, cholesterol, absorption, or cholesterol synthesis. Garlic oil could not be recommended for hypercholesterolemia. The study was criticized for slow-release aspect that has been found to greatly reduce total absorption and because the oil preparation contained a different chemical profile than preparations used in other studies.
Isaacsohn, 1998	Hyperlipidemia (LDL<160 mg/dL; TG <350 mg/dL)	R, PC, PG, MC n=50 (n=28 taking garlic; n=22 taking placebo) subjects on the NCEP Step 1 diet 8 weeks before and during treatment	12 weeks	300 mg, 3x/day	Sapec®, Kwai® garlic powder	No significant lipid or lipoprotein changes between the two groups. Compliance to diet was same for both groups; however, effect of diet on lipid/lipoprotein levels prior to treatment may have influenced treatment. Another factor possibly influencing the results is the alleged change made to the tablets' enteric coating in 1992–1993 (Lawson, 1998).
Lash *et al.*, 1998	Hyperlipidemia in renal transplant patients (TC>185 mg/dl; LDL> 160 mg/dl)	R, PC n=35 (garlic n=19; placebo n=16) (NCEP Step 1 diet during treatment)	12 weeks	680 mg, 2x/day	Pure-Gar®	At 6 weeks, there was a significant decrease from baseline of 14 mg/dL in TC ($p<0.05$) and 12 mg/dL in LDL ($p<0.05$). Authors noted that although garlic showed benefit, patients still required drug therapy to treat hyperlipidemia. They suggested that garlic may be used to decrease the required dosage of HMG-CoA reductase inhibitors.
McCrindle *et al.*, 1998	Hypercholesterolemia in children (TC >185 mg/dL)	R, DB, PC n=30 (garlic n=15; placebo n=15) NCEP Step 2 diet for 6 months prior to treatment	8 weeks	300 mg, 3x/day	Kwai® garlic powder	There was no significant reduction attributed to garlic for cardiovascular risk factors, with the exception of a small increase in apolipoprotein A-I levels. Authors note that adult studies have yielded positive results.
Steiner *et al.*, 1996	Hypercholesterolemia (men) (TC=220–280 mg/dL)	DB, PC, C n=41	6 months, crossed over for 4 months (placed on NCEP Step 1 diet 4 weeks prior to start/ throughout)	3 capsules (800 mg each) 3x/day	Kyolic® AGE capsules vs. placebo capsules	Total cholesterol (TC) levels were reduced 6.1–7% compared to placebo period or baseline ($p=0.0001$), respectively. No difference noted for total glycerides (TG) or HDL ($p=0.004$). LDL decreased 4% and systolic blood pressure (SBP) decreased 5.5% ($p=0.0001$) with the garlic and modes decreased in diastolic blood pressure (DBP). Authors concluded AGE garlic supplementation has beneficial effects on lipid profile and BP in moderately hypercholesterolemic patients.
Yeh *et al.*, 1995	Hypercholesterolemia (TC=220–285 mg/dL)	DB, PC, R n=34 (garlic n=17; placebo n=17) men (35–55 years old)	5 months	3 capsules, (800 mg each) 3x/day	Kyolic® AGE capsules vs. placebo capsules containing common food ingredient	At 4th and 5th month, TC levels in AGE group 6% and 7% lower, respectively, than baseline value and no change in placebo group. Plasma HDL-cholesterol and triglyceride levels not altered by AGE or placebo. Compared with placebo, LDL-cholesterol level significantly lower in AGE group (145 ± 25 vs. 165 ± 24 mg/dl). AGE supplementation has significant mild cholesterol lowering effect in hypercholesterolemic men.
De A Santos and Johns, 1995	Garlic powder vs. garlic oil on blood lipids, blood pressure, and well-being	R, O, PG, Cm, n=70 (garlic powder n=36; or garlic oil n=34)	16 weeks	200 mg, 3x/day	Garlic powder: Kwai® (tablet), Garlic oil: Höfel's® Original Garlic Oil Capsules	Lipid-lowering effect for garlic powder=11% vs. 3% for oil. LDL lowered by 16% vs. 1% respectively. HDL did not change significantly and TG did not change. Also noted was a decrease in blood pressure with garlic powder but not for oil. Well-being assessment improved for powder but not for oil. Garlic powder appears to be superior to oil in reducing cholesterol, BP, and improved well-being.

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Clinical Studies on Garlic (*Allium sativum* L.) (cont.)

Cardiovascular (cont.)

Hyperlipidemia/Hypercholesterolemia/Hypertension/Related Risk Factors (cont.)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Simons *et al.*, 1995	Hypercholesterolemia (mild to moderate) (5.5–8.05 mmol/L)	R, DB, PC, CO n=28	12 weeks after 28 day baseline dietary period; 28 day washout at end	300 mg, 3x/day	Kwai® garlic powder	No demonstrable effect of garlic on oxidizabilty of LDL, on ratio of plasma lathosterol/cholesterol (a measure of cholesterol synthesis), nor on LDL receptor expression in lymphocytes. No effect on ingestion of lipids and lipoproteins.
Steiner and Lin, 1994	Hypercholesterolemia (TC=230–290 mg/dL)	DB, CO, R n=45 men (30–70 years old)	10 months	700 mg, 3 capsules, 3x/day	Kyolic® AGE capsules vs. placebo capsules	66% of subjects in garlic group showed modest reduction (about 8%) of total and LDL cholesterol but no change in HDL. Significant reductions in measured platelet adhesion (34–58%) and aggregation (10–25%). Study suggests that AGE supplementation has beneficial effects on lipids, especially platelets, that may lead to cardiovascular risk reduction.
Jain *et al.*, 1993	Serum lipids, lipoproteins, glucose, and blood pressure	R, DB, PC n=42	12 weeks	300 mg, 3xday, or placebo	Garlic powder in tablet form	Experimental group experienced a 6% reduction in TC ($p<0.01$) vs. placebo group (1%) reduction. LDL decreased 11% and 3% respectively ($p<0.05$). No changes in HDL, TG, serum glucose, or blood pressure noted (subjects were normotensive).
Grünwald *et al.*, 1992	Hypercholesterolemia (TC>6.5 mmol/L)	DB, MC n=48	18 weeks	200 mg, 3x/day Subjects maintained a normal diet and medications	Kwai® garlic powder	After garlic treatment and compared to baseline, mean serum TC decreased by 8% ($p<0.001$); LDL decreased by a non-significant 5%; HDL increased by 5%; LDL: HDL improved by 12% ($p<0.05$); TG levels decreased by a non-significant 11%. 23 patients with mild hypertension experienced a significant decrease of 7% in SBP ($p<0.05$) and a non-significant 4% in DBP.
Holzgartner *et al.*, 1992	Hyperlipoproteinemia (TC or TG >250 mg/ml) garlic vs. Bezafibrate	R, DB, MC, Cm n=98 (6-week prephase treatment w/placebo and NCEP Step I diet)	12 weeks (NCEP Step I diet maintained throughout study)	900 mg/day or 600 mg Bezalfibrate/ day	Garlic powder preparations equivalent to Sapec®, Kwai® garlic powder	Compared to baseline, both medications caused a significant decrease in TC (26%) ($p<0.001$), LDL (32%) ($p<0.001$), and TG (30%) ($p<0.01$), as well as a significant increase in HDL (51%) ($p<0.001$) with no difference between their efficacies. No differences were observed between the two regimens.
Rotzsch *et al.*, 1992	Alimentary hypertriglyceridemia (after intake of fatty meals)	R, DB, PC n=24	6 weeks	300 mg/day or placebo and fatty meal	Sapec®, Kwai® garlic powder; fatty meal contained 100g butter	The postprandial increase of TG was reduced significantly in garlic group, and was up to 35% less compared to placebo. HDL-2 cholesterol tended to increase with garlic more than placebo.
Auer *et al.*, 1990	Mild hypertension (DBP 95–104 mmHg; TC >250; TG>200)	R, DB, PC, C n=47 (garlic n=24; placebo n=23) (n=21 taking blood pressure medication)	12 weeks (after 7 week acclimation period)	200 mg/day or placebo	Kwai® garlic powder	Results indicated 13% decrease in DBP in garlic group vs. 4% for placebo ($p<0.01$). SBP decreased by 11% in garlic compared with 5% in the placebo group ($p<0.05$). Serum cholesterol and TG were significantly decreased after 8 and 12 weeks in garlic group vs. placebo ($p<0.05$).
Mader *et al.*, 1990	Hyperlipidemia (TC >200mg/dL)	R, DB, PC, PG, MC n=221 (garlic n=111; placebo n=110)	16 weeks	200 mg/day or placebo	Kwai® garlic powder	Experimental group experienced a 12% reduction in TC vs. a 3% reduction in placebo group ($p<0.001$). TG decreased by 17% vs. 2% respectively ($p<0.0001$). The best effect was noted in patients with TC levels 251–300 mg/dL.
Vorberg *et al.*, 1990	Hypercholesteriolemia	R, DB, PC, PG n=40 (garlic n=20; placebo n=20)	16 weeks	300 mg, 3x/day	Sapec®, Kwai® garlic powder	Garlic group resulted in a significantly lower TC ($p<0.001$), TG ($p<0.05$), BP ($p<0.001$), than placebo. A self-evaluation revealed a greater feeling of "well being" ($p<0.05$).

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Cardiovascular (cont.)

Hyperlipidemia/Hypercholesterolemia/Hypertension/Related Risk Factors (cont.)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Lau, *et al.*, 1987	Hypercholesterolemia and hypertriglycerides	DB, C, CC n=15	6 months	1 g/day	Kyolic® AGE capsules	Serum cholesterol level (220–440 mg/dl) significantly dropped (12–31%) with AGE compared to baseline. Serum LDL and triglycerides were also significantly reduced ($p<0.05$) with AGE.
Bordia, 1981	Blood lipids in subjects with coronary heart disease	O (n=20) healthy volunteers or (n=62) patients with coronary heart disease	10 months	0.25 mg/kg of body weight/day or placebo	Garlic essential oil in gelatin capsules	Patients taking garlic experienced a decrease in serum cholesterol ($p<0.05$) and LDL ($p<0.05$), while an increase was observed in the HDL fraction ($p<0.05$).

Arterial and Fibrinolytic Activity

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Steiner and Li, 2001	Effects on platelet function	DB, CO, PC, R n=34 normal healthy men and women	44 weeks (6-week baseline period; 18-week supplementation, 18-week crossover; 2-week washout)	3 capsules (800 mg each) 3x/day 1st 6 weeks; 800 mg, 6x/day 2nd 6 weeks; 800 mg, 9x/day 3rd 6 weeks	Kyolic® AGE capsules vs. placebo capsules	Compared with baseline and placebo, threshold level of platelet aggregation was significantly increased, i.e., AGE significantly ($p<0.05$) inhibited platelet aggregation, especially induced by collagen and epinephrine. Adherence of platelets inhibited by AGE in dose-dependent manner. AGE exerted selective inhibition on platelet aggregation and adhesion, suggesting potential use as cardiovascular disease prevention.
Koscielny *et al.*, 1999	Arterial plaque (in patients with advanced atherosclerotic plaque)	R, DB, PC n=152	4 years	300 mg, 3x/day	Kwai® garlic powder	In placebo the atherosclerotic plaque (in carotid and femoral artery) increased by 15.6% over 4 years while decreasing 2.6% in experimental group ($p<0.0001$). Garlic diminished the age-related decrease in plaque volume by 6–13% over 4 years ($p<0.001$). Assessed by high-resolution ultrasound. Results substantiate a preventive and curative role for garlic powder for atherosclerosis.
Breithaupt-Grogler, 1997	Age-related stiffening of the aorta (healthy adults)	E, CS, OB n=202 (matching pairs technique)	≥2 years	≥300 mg/day	Standardized garlic powder	Pressure-standardized elastic vascular resistance was lower in garlic groups than age-matched controls ($p<0.0001$). Pulse wave velocity (PWV) correlated with age (r=0.44 garlic, r=0.52 control) and systolic blood pressure (SBP) (r=0.48 garlic group, r=0.54 control group) for both groups, but in garlic group an increase in age or SBP was associated with a smaller rise in PWV vs. controls. No difference noted in blood pressure, heart rate, and plasma lipid levels in both groups. Chronic garlic powder consumption attenuated age-related increase in aortic stiffness.
Kiesewetter *et al.*, 1993a	Platelet aggregation (juvenile ischemic attack)	DB, PC, PG n=60	4 weeks (following a 4-week washout period)	200 mg, 4x/day or placebo	Kwai® garlic powder	A significant decrease ($p<0.01$) in circulatory platelet aggregates (down 10.3%) and spontaneous platelet aggregates (down 56.3%) was observed in garlic group. Garlic group also decreased in DBP, plasma viscosity, and serum cholesterol.
Kiesewetter *et al.*, 1991	Platelet aggregation	DB, PC n=120	4 weeks	400 mg, 2x/day or placebo	Garlic powder	Observations in garlic group include spontaneous platelet aggregation disappearance, increase of 47.6% microcirculation of the skin, 3.2% decrease in plasma viscosity, mean DBP decrease from 74 to 67 ($p<0.05$), and a drop in the mean fasting blood glucose concentration from 89.4 to 79.

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Anticancer/Chemoprevention

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Dimitrov and Bennink, 1997	Effect on arachidonic acid metabolism	PS, O n=8 healthy female volunteers	3 months	10 mL extract/day mixed with orange or V8 juice in morning	Kyolic® aged garlic hydroalcoholic liquid extract	Compared to baseline, after 3 months of taking Kyolic® substantial decrease in serum PGE2 levels in majority of subjects. Results indicate that ethanol-water soluble extract is capable of modulating PGE2 and PGF2a.
Witte *et al.*, 1996	Colon cancer	E, CC n=488	4 years	≥3 servings/week	Serving size unspecified	A reduction of 37% occurrence in pre-cancerous cells and colorectal polyps was observed. (Odds ratio = 0.63.)
Gwilt *et al.*, 1994	Effect on metabolism of acetamino-phen	O n=16 males (healthy, non-smoking)	3 months	10 ml extract/day mixed with 120 ml orange juice	Kyolic® aged garlic hydroalcoholic liquid extract plus acetamin-ophen (500 mg Tylenol®)	Garlic treatment had no discernible effect on oxidative metabolism, but was associated with slight increase in sulfate conjugation of acetaminophen. Study suggests that AGE has limited potential as a chemopreventive agent.
Steinmetz *et al.*, 1994	Colon cancer	E, CH n=41,837	5 years	≥ 1 servings/week	Unspecified as to the quantity of a serving size	The study showed that risk of colon cancer in women ages 55–69 decreased with garlic consumption (rr=0.68).
You *et al.*, 1989	Stomach cancer	E n=564 patients with stomach cancer, n=1,131 controls	15 years	0 kg/year; 0.1–1.5 kg/y; >1.5 kg/y	Raw and cooked garlic	Significant trends were shown for the decrease of stom-ach cancer with garlic use. Odds ratio (95% CI) for highest compared with lowest garlic consumption was 0.7 (0.4–1.0, p=0.03).

Other

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Rozenfeld *et al.*, 2000	Bleeding potential of combined garlic and warfarin therapy	DB, PC, R n=8 patients (INR therapeutic for at least 2 months)	4 weeks	1,200 mg/day or placebo	Kyolic® AGE capsules	All patients took Coumadin®. No INR differences between groups noted (p>0.05). Compared to baseline, no significant changes in INR values within each group (p>0.05). No patients developed urine or stool bleeding. Kyolic® did not worsen side effects of Coumadin®.
Okuhara, 1994	Peripheral circulation	Cm, CO, R n=12 healthy male volunteers	5 months (Jan~May 1994)	Single-admin-istration test: 1.6 ml GE or GEC/day or continuous administration test: 0.8 ml GE or GEC 2 x/day	Kyolic® aged garlic hydroal-coholic liquid extract (GE) vs. heat-treated liquid prepara-tion of garlic (GEC)	After single administration, skin temperatures in GE (garlic) group peaked at 60 minutes on backs of hands (p<0.01) and 90 minutes on backs of feet (p<0.01). In GEC (control) group, peaked at 30 minutes on backs of hands and feet. After 14 days continuous use, higher skin temperatures in GE group on backs of hands and feet and on only backs of feet in GEC group. Study suggests improved blood flow with GE.
Kiesewetter *et al.*, 1993b	Intermittent claudication (Peripheral Arterial Occlusive Disease Stage II)	DB, PC n=80	12 weeks	200 mg, 4x/day or placebo	Kwai® garlic powder	A significant increase (p<0.05) was observed in walking distance by the 5th week and correlated to a simultane-ous decrease in spontaneous platelet aggregation in gar-lic group vs. placebo. Garlic group also had decrease in diastolic blood pressure (DBP), plasma viscosity, and serum cholesterol.
Abdullah *et al.*, 1989	Effects on natural killer (NK) cell activity in HIV+ patients	PS n=7	12 weeks	5 g/day 1st 6 weeks; 10 g/day 2nd 6 weeks	Aged processed garlic prepara-tion: Special Garlic Preparation (SGP)	After 6 weeks, 6 of 7 qualified patients had normal NK activity, and all had normal NK activity at 12 weeks. Helper/suppressor ratio improved in 4 of 7 patients. Conditions of diarrhea, genital herpes, candidiasis and pansinusitis with recurrent fever also improved during the study.

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