NUTRITION REVIEWS

Special Article

Effect of garlic on serum lipids: an updated meta-analysis

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Hypercholesterolemia is associated with an increased risk of heart disease. The effect of garlic on blood lipids has been studied in numerous trials and summarized in meta-analyses, with conflicting results. This meta-analysis, the most comprehensive to date, includes 39 primary trials of the effect of garlic preparations on total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides. The findings suggest garlic to be effective in reducing total serum cholesterol by 17 ± 6 mg/dL and low-density lipoprotein cholesterol by 9 ± 6 mg/dL in individuals with elevated total cholesterol levels (>200 mg/dL), provided garlic is used for longer than 2 months. An 8% reduction in total serum cholesterol is of clinical relevance and is associated with a 38% reduction in risk of coronary events at 50 years of age. High-density lipoprotein cholesterol levels improved only slightly, and triglycerides were not influenced significantly. Garlic preparations were highly tolerable in all trials and were associated with minimal side effects. They might be considered as an alternative option with a higher safety profile than conventional cholesterol-lowering medications in patients with slightly elevated cholesterol.

INTRODUCTION

Elevated serum lipid levels are associated with an increased risk of cardiovascular disease, particularly with coronary events and atherosclerosis.[1–3] Current medical practice includes the prescription of lipid-lowering medication such as statins. General practice data from 2009 indicate that almost one-quarter of adult patients (23.8%) were prescribed antihyperlipidemic medicines, 88.4% of which were statins.[4] While effective in lowering cholesterol and triglyceride levels, statins have been shown in a considerable number of patients to trigger adverse effects, including myalgia, muscle weakness, neuropathy, and cognitive dysfunction, and to increase the risk of diabetes.[5–10]

Garlic preparations have been linked to cardiovascular benefits.[11,12] The effect of garlic on cholesterol has been investigated in numerous trials and summarized in several meta-analyses, with variable results.[13–19] The meta-analysis presented here is the most comprehensive to date and includes earlier as well as more recent trials investigating the effects of single-product garlic preparations versus placebo. The effects of garlic on total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglyceride levels are summarized, and statistical oversights in some previous meta-analyses are rectified; for example, only the first phase of crossover trials without a washout period is included, or only one of multiple active trial arms versus placebo is included in this meta-analysis. The effect of potential confounding variables such as duration of treatment, type of garlic preparation, and baseline cholesterol levels was explored in subgroup analyses, and robustness of results was tested by sensitivity analysis.

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METHODS

Search strategy

The Medline and Cochrane databases and Google Scholar were searched for randomized, placebo-controlled human trials investigating the effect of garlic on cholesterol and published between 1955 and December 2011 in English or German using the following search terms: garlic, allium sativum, allicin, cholesterol, hyperlipidemia, and lipid. Reference lists of published studies and review articles were also searched manually.

Selection of trials

Trials were included in the meta-analysis if they were ≥2 weeks in duration, contained a true placebo control group, were conducted in adult subjects, and tested garlic as a single active substance. Data on total serum cholesterol LDL cholesterol, HDL cholesterol, and triglyceride levels at baseline and at the end of the trial were collated. Authors of recent trials were contacted to obtain unreported data needed for pooling.[20] Trials were excluded from meta-analysis if data required for pooling were missing (i.e., baseline mean and standard deviation [SD], end mean and SD, or change by group) or if studies involved pregnant participants or patients with conditions that required cholesterol-lowering medical treatment.

Data extraction and quality assessment

Data were abstracted and quality assessed independently by three investigators (KR, CT, PF) using guidelines published by the Cochrane Collaboration.[21] Any disagreement was resolved by discussion between the authors. Quality was assessed independently by two investigators (KR, CT) on the basis of randomization, blinding, loss to follow-up, funding sources, and compliance. High quality was given a score of 1 and low quality a score of 0 for each of the five items, with a maximum quality score of 5. Quality assessment was useful for sensitivity analysis, and trials of low quality (score ≤2) or trials with high loss-to-follow-up (>20% attrition) were excluded, since either is likely to have influenced outcome measures.

Analysis

Meta-analyses were conducted using the Cochrane Program Review Manager version 5.1.6.[22] The generic inverse variance model and random effects were used, owing to high heterogeneity between trials. Mean differences and standard errors (SE) between garlic groups and control groups were calculated at the end of the trial, with the mean difference adjusted for baseline differences between the intervention groups. Heterogeneity was assessed by the I^2 statistics. Heterogeneity was considered low if $I^2 < 30\%$, moderate if $I^2 = 30 - 75\%$, and high if $I^2 > 75\%$.[21]

Blood lipid levels were collated in mg/dL. If cholesterol levels (TC, HDL, LDL) or triglyceride levels were published in mmol/L, amounts were multiplied by a factor of 38.7 for cholesterol and 88.6 for triglycerides to convert to mg/dL. Mean differences were calculated as follows: Effect mean = (end $\text{mean}_{\text{garlic}}$ − end $\text{mean}_{\text{control}}$) − (mean $\text{baseline}_{\text{garlic}}$ − mean $\text{baseline}_{\text{control}}$). SE of mean differences (end $\text{mean}_{\text{garlic}}$ − end $\text{mean}_{\text{control}}$) were calculated using the following formula: $SE = SQRT(SD_{garlic}^2/n_{garlic}) + (SE_{control}^2/n_{control})$ for parallel trials, and $SE = SQRT(SD_{garlic}^2 + SD_{control}^2 - 2{*}0.25 {*} SD_{garlic} {*} SD_{control})/n)$ for crossover trials, where SQRT = square root, SD = standard deviation at end/follow-up, and n = number of participants.

Meta-analyses of all eligible trials on the effect of garlic on total cholesterol (TC), LDL cholesterol, HDL cholesterol, and triglyceride were conducted, as were subgroup analyses by duration (2–8 weeks [short] or >8 weeks [long]), by TC baseline (<200 mg/dL or ≥200 mg/dL), by type of garlic supplement (garlic powder, enteric-coated garlic powder, aged garlic extract, garlic oil, or raw garlic), and by industry funding.

Sensitivity analysis of studies with multiple active trial arms was conducted, whereby only one arm of an active product (e.g., garlic powder or garlic oil) was compared with placebo. Further sensitivity analysis was performed by excluding trials of low quality and with high loss-to-follow-up, or by excluding trials in which a proportion of participants were on lipid-lowering medication.

Additionally, results are compared with those of previous meta-analyses, available data on active ingredients in garlic preparations are provided, and side effects reported by trial participants are summarized.

Publication bias or small study effect was assessed by Begg's funnel plots.[23]

RESULTS

Summary of included studies

A total of 63 publications were assessed for eligibility (Figure 1). A total of 39 trials fit inclusion criteria for meta-analysis, of which 37 reported sufficient data on total cholesterol levels, 26 reported LDL cholesterol data, 30 reported HDL cholesterol data, and 32 reported triglyceride data (Table 1).[24–61]

Twenty-five trials (24 articles and 1 trial arm) were excluded for the following reasons: 1) trial reported insuf-

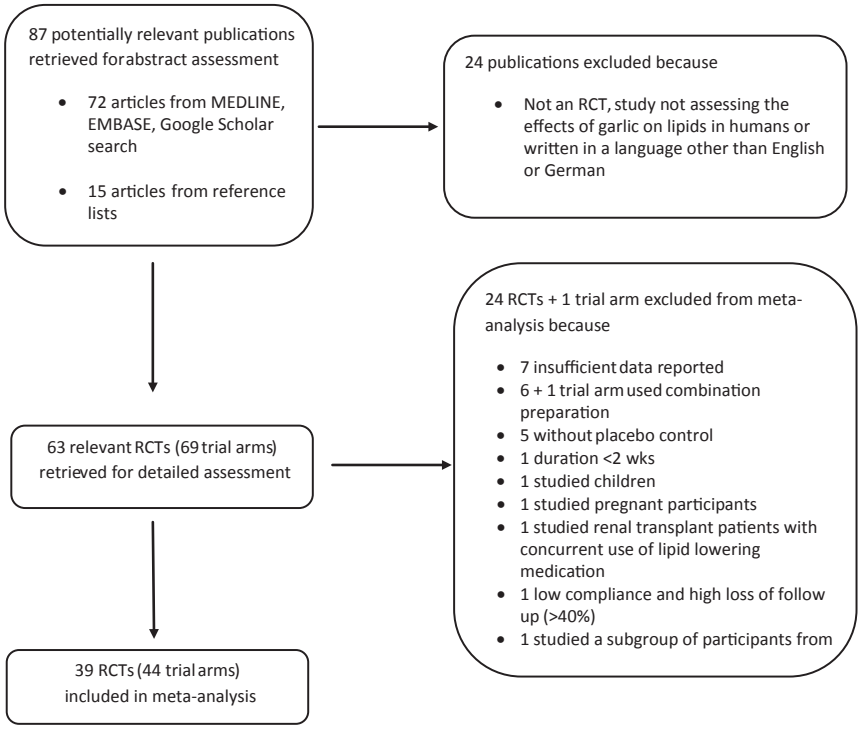

Figure 1 **Flow diagram for selection of trials.**
Abbreviations: RCT, randomized controlled trial.

ficient data for pooling ($n = 7$)[62–68]; 2) a combination preparation was tested ($n = 6 + 1$ study arm)[69–74]; 3) trial was not placebo controlled ($n = 5$)[75–79]; 4) trial was less than 2 weeks in duration ($n = 1$)[80]; 5) trial involved children ($n = 1$),[81] pregnant women ($n = 1$),[82] or renal transplant patients ($n = 1$)[83]; 6) trial reported low compliance and high loss-to-follow-up ($n = 1$)[84]; or 7) trial analyzed a subgroup of participants from a larger trial included in the meta-analysis ($n = 1$)[85] (Table 2).

The 39 trials included in the meta-analysis involved a total of 2,298 participants with a mean age of 49.5 years (range, 20–60 years) (Table 1). Most trials employed a parallel study design ($n = 32$), although five trials used a crossover design. While two trials reportedly used a crossover design, only parallel data of the first phase of these studies were useful for meta-analysis.[29,55] The majority of trials investigated garlic powder, ($n = 29 + 2$ arms), while six trials used garlic oil, six used aged garlic extract, and three used raw garlic. Trials ranged 2–52 weeks in duration: 9 trials ranged 2–8 weeks, and 30 trials were longer than 8 weeks. Ranges of daily dosages were as follows: garlic powder, 600–5,600 mg/day; garlic oil, 9–18 mg/day; aged garlic extract, 1,000–7,200 mg/day; and raw garlic, 4–10 g/day. Dosages of garlic preparations are not directly comparable, as active ingredients and bioavailability vary considerably between different types of preparations (powder, oil, aged extract, raw). Furthermore, dosage of the active ingredient can also vary within one type, depending on brand and processing.

Mean total serum cholesterol levels of participants were elevated at baseline in the majority of trials ($TC_{baseline} \geq 200$ mg/dL, $n = 29$), whereas eight trials recruited participants with total serum cholesterol levels of less than 200 mg/dL. Participants in all but three trials[31,54,57] had not taken lipid-lowering prescription medication for at least 4–12 weeks before the trial. Budoff et al.[54] and Williams et al.[57] included patients with known coronary artery disease and some patients on lipid-lowering medication. In the trial by Budoff et al.,[54] the garlic and control groups were matched by participants using statins 10–40 mg per day, while no details were reported in Williams et al.[57] In the trial by Mader,[31] only a small proportion of participants were taking lipid-lowering medication (4% in the garlic group and 2% in the control group).

Quality of trials was generally adequate. All but two trials[33,45] reported adequate randomization, all but two trials[24,33] testing raw garlic were double-blinded placebo-controlled trials, and two trials[41,51] had greater than 20% loss to follow-up. Compliance was assessed and reported as high in 15 trials, and industry-funded support was reported in 13 trials (Table 3).

Table 1 **Characteristics of trials included in the meta-analysis.**

Reference	No. of subjects (garlic/ control)	Study design	Garlic type	Brand	Dose of product (mg/day)	No. of tablets or capsules[a] per day	Dose of active ingredient per day	Duration of trial (weeks)	Total cholesterol, garlic group		Total cholesterol, control group	
									Baseline (mg/dL)	End (mg/dL)	Baseline (mg/dL)	End (mg/dL)
Bhushan et al. (1979)[24]	15/10	p	RG	NCP	10,000	NA	NR	8.5	223	190	206	205
Bordia (1981)[25]	33/29	p	GO	NCP	0.25/kg	2	NR	40	300	230	280	280
Barrie et al. (1987)[26]	20/20	c	GO	NCP	18	NR	NR	4	195	180	193	190
Lau et al. (1987)[27]	15/12	p	AGE	Kyolic®	1,000	4	1.2 mg SAC	24	313	262	303	292
Sitprija et al. (1987)[28]	17/16	p	GP	NCP	700	2	NR	4	219	229	237	240
Plengvidhya et al. (1988)[29]	16/14	p	GP	NCP	700	2	NR	8	266	234	295	269
Auer et al. (1990)[30]	24/23	p	GP	Kwai®	600	2	7.8 mg alliin[b]	12	268	230	267	247
Mader (1990)[31]	111/110	p	GP	Kwai	800	4	10.4 mg alliin	16	266	235	262	255
Vorberg & Schneider (1990)[32]	20/20	p	GP	Kwai®	900	NR	11.7 mg alliin[b]	16	294	233	288	278
Gadkari & Joshi (1991)[33]	30/20	p	RG	NCP	10,000	NA	NR	8.5	213	180	212	212
Rotzsch et al. (1992)[34]	12/12	p	GP	Kwai®	900	3	11.7 mg alliin[b]	6	NR	NR	NR	NR
Jain et al. (1993)[35]	20/22	p	GP	Kwai®	900	3	11.7 mg alliin	12	262	247	276	274
Kiesewetter et al. (1993)[36]	32/32	p	GP	Kwai®	800	4	10.4 mg alliin[b]	12	267	234	264	253
Phelps & Harris (1993)[37]	10/10	c	GP	Kwai®	600	6	7.8 mg alliin[b]	2	176	175	174	173
DeA Santos & Gruenwald (1993)[38]	25/27	p	GP	Kwai®	900	NR	11.7 mg alliin	24	268	244	273	261
Saradeth et al. (1994)[39]	31/37	p	GP	Kwai®	600	NR	7.8 mg alliin	15	223	214	217	218
Simons et al. (1995)[40]	28/28	c	GP	Kwai®	900	3	11.7 mg alliin[b]	12	260	253	260	251
Neil et al. (1996)[41]	57/58	p	GP	Kwai®	900	3	11.7 mg alliin	24	269	267	270	273
Adler & Holub (1997)[42]	12/11	p	GP	Kwai®	900	3	11.7 mg alliin[b]	12	253	224	250	251
Yeh et al. (1997)[43]	16/16	p	AGE	Kyolic®	7,200	9	NR	20	246	228	243	245
Berthold et al. (1998)[44]	25/25	c	GO	Tegra®	10	NR	4,000 U allicin eq	12	291	NR	291	NR
Bordia et al. (1998)[45]	30/30	p	GO	NCP	4[c]	4	NR	12	253	201	253	249
Isaacsohn et al. (1998)[46]	28/22	p	GP	Kwai®	900	3	11.7 mg alliin[b]	12	274	279	250	250
Rahmani et al. (1999), trial arm A[47]	30/22	p	GP	Garlet®	1,200	3	NR	12	274	268	267	267
Rahmani et al. (1999), trial arm B[47]	21/22	p	GP	Garlet®	2,400	6	NR	12	259	238	267	267
Rahmani et al. (1999) trial arm C[47]	20/22	p	GP	Garlet®	3,600	9	NR	12	258	255	267	267
Superko & Krauss (2000)[48]	25/25	p	GP	Kwai®	900	3	11.7 mg alliin[b]	12	250	278	239	261
Zhang et al. (2000)[49]	14/13	p	GO	Cardiomax®	12.3	3	NR	16	186	184	178	175
Kannar et al. (2001)[50]	20/23	p	GP	NCP	880	4	9.6 mg allicin pt	12	286	245	275	280
Zhang et al. (2001), trial arm A[51]	19/21	p	GO	Cardiomax®	9	2	8.2 mg allyl sulfide	11	186	176	190	188
Zhang et al. (2001), trial arm B[51]	20/21	p	GP	Garlicin®	1,000	2	7.8 mg allicin pt	11	166	163	190	188
Peleg et al. (2003)[52]	13/20	p	GP	Inod'Ail	22,400[d]	4	22.4 mg alliin	16	263	260	275	268
Satitvipawee et al. (2003)[53]	70/76	p	GP	NCP	333	1	5.6 allicin pt	12	257	255	265	263
Budoff et al. (2004)[54]	9/10	p	AGE	Kyolic®	1,220	4 ml[e]	1.2 mg SAC	48	176	183	199	212
Tanamai et al. (2004)[55]	45/45	p	GP	NCP	900	NR	5 mg allicin pt	13	284	266	284	267
Ashraf et al. (2005)[56]	35/35	p	GP	Garlex®	600	2	15.6 mg alliin	12	228	201	220	218
Williams et al. (2005)[57]	15/15	c	AGE	Kyolic®	2,400	4	2 mg SAC[b]	2	166	166	170	166
Macan et al. (2006)[58]	22/26	p	AGE	Kyolic®	3,050	10 ml[e]	14.7 mg SAC	12	184	192	184	180
Gardner et al. (2007), trial arm A[59]	42/43	p	RG	NCP	4,000	NA	NR	24	NR	NR	NR	NR
Gardner et al. (2007), trial arm B[59]	41/43	p	GP	Garlicin®	4,000	4	3.2 mg allicin pt	24	NR	NR	NR	NR
Gardner et al. (2007), trial arm C[59]	42/43	p	AGE	Kyolic®	4,000	6	1.5 mg SAC	24	NR	NR	NR	NR
Sobenin et al. (2008)[60]	23/19	p	GP	Allicor®	600	2	7.8 mg allicin pt	12	270	248	273	280
Sobenin et al. (2010)[61]	26/25	p	GP	Allicor®	300	2	3.9 mg allicin pt	52	270	236	253	242
Han et al. (2011)[20]	22/22	p	GP	NCP	1,000	2	0.75 mg SAC	8	201	199	183	176

[a] Garlic powder, aged garlic extract powder, or garlic oil.
[b] Estimation based on standardized formula; active ingredient not reported in publication.
[c] Estimate of volume of garlic oil extracted from 2 g of raw garlic.
[d] Dosage, as reported in Peleg et al.,[52] likely too high by a factor of 10.
[e] Volume of aged garlic extract liquid.
Abbreviations: AGE, aged garlic extract; c, crossover trials; eq, equivalent (allicin equivalent measured by adding water to garlic product containing allicin and alliinase); GO, garlic oil; GP, garlic powder; NA, not applicable; NCP, noncommercial product; NR, not reported; p, parallel trials; pt, potential; RG, raw garlic; SAC, S-allylcysteine.

Table 2 **Characteristics of trials excluded from the meta-analysis.**

Reference	No. of subjects (garlic/ control)	Study design	Garlic type	Duration of trial (weeks)	Reason for exclusion
Kandziora (1988)[62]	20/20	p	GP	12	Insufficient data
Kiesewetter et al. (1991)[63]	30/30	p	GP	5	Insufficient data
Luley et al. (1986)[64]	31/51	c	GP	6	Insufficient data
Mansell et al. (1996)[65]	30/30	p	GP	12	Insufficient data
Turner et al. (2004)[66]	31/32	p	GP	12	Insufficient data
Kojuri et al. (2007)[67]	50/50	p	GP	6	Insufficient data
van Doorn et al. (2006)[68]	28/30/26	p	GP/atorvastatin/placebo	12	Insufficient data
Adler & Holub (1997)[42]; trial arm i	11/10	p	GP + fish oil	12	Combination preparation in additional study arm
Czerny & Samochowiec (1996)[69]	50/50	p	GP + soy lecithin	16	Combination preparation
Lutomski (1984)[70]	44/38	p	GP	12	Combination preparation
Morcos (1997)[71]	40/40	c	GP/fish oil	4	Combination preparation
Gardner et al. (2001)[72]	33/18	p	GP + Fabaceae/Brassicaceae extract	12	Combination preparation
Jeyaraj et al. (2005)[73]	16/16	p	GO + fish oil	8.5	Combination preparation
Budoff et al. (2009)[74]	30/28	p	AGE + vitamins/amino acids	52	combination preparation
Schmidt (1991)[75]	34/33	p	GP vs. benzofibrate	12	No placebo control
Holzgartner et al. (1992)[76]	47/47	p	GP vs. benzofibrate	12	No placebo control
DeA Santos & Johns (1995)[77]	36/34	p	GP vs. GO	16	No placebo control
Dhawan & Jain (2004)[78]	20/20	p	GO	8	No placebo control, hypertensives vs normotensives
Jabbari et al. (2005)[79]	25/25	p	RG	8	No placebo control, RG chewed vs RG swallowed
Jung & Kiesewetter (1991)[80]	10	c	GP	2 h, 5 h	Acute, <2 weeks
McCrindle et al. (1998)[81]	15/15	p	GP	8	Children (8–18 years)
Ziaei et al. (2001)[82]	50/50	p	GP	8	Pregnant subjects
Lash et al. (1998)[83]	35/35	p	GP + medication	12	Renal transplant patients, concurrent use of lipid-lowering medication
Steiner et al. (1996)[84]	41/41	c	AGE	24	Low compliance and loss to follow-up (>40%), no washout
Byrne et al. (1999)[85]	20/11	p	GP	24	Subgroup from larger trial, Neil et al. (1996)[41]

Abbreviations: AGE, aged garlic extract; c, crossover trial; GO, garlic oil; GP, garlic powder; h, hours; NR, not reported; p, parallel trial; RG, raw garlic.

Table 3 **Quality assessment of trials included in the meta-analysis.**

Reference	Total quality score (maximum possible = 5)	Randomization: (1 = randomized, 0 = nonrandomized)	Blinding: (1 = double blind, 0 = single blind)	Loss to follow-up: (1 = < 20%, 0 = ≥ 20%)	Compliance: (1 = >80%, 0 = ≤ 80%)	Funding score: (1 = no sponsor involved, 0 = sponsored involved[a])	Diet modification[b]
Bhushan et al. (1979)[24]	3	1	0	1: none	0	1	Onion intake prohibited
Bordia (1981)[25]	4	1	1	1: 9% (6 of 68)	0	1	No
Barrie et al. (1987)[26]	4	1	1	1: none	0	1	Garlic intake limited
Lau et al. (1987)[27]	4	1	1	1: 16% (27 of 32)	1	1	No
Sitprija et al. (1987)[28]	4	1	1	1: none	0	1	Dietary control – not defined
Plengvidhya et al. (1988)[29]	4	1	1	1: none	0	1	Diet containing an appropriate amount of carbohydrate, protein, and fat
Auer et al. (1990)[30]	4	1	1	1: none	0	1	No
Mader (1990)[31]	4	1	1	1: 15% (40 of 261)	0	1	No
Vorberg & Schneider (1990)[32]	4	1	1	1: none	0	1	No
Gadkari & Joshi (1991)[33]	2	0	0	1: none	0	1	No
Rotzsch et al. (1992)[34]	3	1	1	1: none	0	0	No
Jain et al. (1993)[35]	3	1	1	1: none	0	0	No
Kiesewetter et al. (1993)[36]	4	1	1	1: 20% (16 of 80)	0	1	No
Phelps & Harris (1993)[37]	4	1	1	1: none	0	1	No
DeA Santos & Gruenwald (1993)[38]	3	1	1	1: 13% (8 of 60)	0	0	Low-fat/low-cholesterol diet
Saradeth et al. (1994)[39]	4	1	1	1: 5% (4 of 72)	0	1	No
Simons et al (1995)[40]	4	1	1	1: 7% (29 of 31)	1	0	Intake of garlic or other nutritional supplements prohibited
Neil et al. (1996)[41]	3	1	1	0: 28% (16 of 56)	1 (>75%)	0	Dietary run-in period, advice on lowering fat intake if high cholesterol
Adler & Holub (1997)[42]	5	1	1	1: 8% (4 of 50)	1	1	No
Yeh et al. (1997)[43]	3	1	1	1: 6% (2 of 34)	0	0	No
Berthold et al. (1998)[44]	5	1	1	1: none	1 (98.4%)	1	No
Bordia et al. (1998)[45]	3	0	1	1: none	0	1	No
Isaacsohn et al. (1998)[46]	4	1	1	1: 16% (8 of 50)	1	0	Restricted fat diet
Rahmani et al. (1999)[47]	5	1	1	1:14% (93 of 108)	1 (>90%)	1	No
Superko & Krauss (2000)[48]	3	1	1	1: none	0	0	American Heart Association Step I diet
Zhang et al. (2000)[49]	4	1	1	1:10% (3 of 30)	1	0	No
Kannar et al. (2001)[50]	4	1	1	1: 7% (43 of 46)	1	0	Australian National Heart Foundation guidelines
Zhang et al. (2001)[51]	3	1	1	0:27% (14 of 51 in a) 0:32% (17 of 53 in b)	1	0	No
Peleg et al. (2003)[52]	5	1	1	1: 15% (6 of 39)	1 (90%)	1	American Heart Association Step I diet
Satitvipawee et al. (2003)[53]	5	1	1	1: 7% (11 of 147)	1 (82%)	1	National Cholesterol Education Program step I diet
Budoff et al. (2004)[54]	4	1	1	1: 17% (4 of 23)	1	0	Garlic intake prohibited
Tanamai et al. (2004)[55]	4	1	1	1:13% (16 of 116)	0	1	Dietary control and physical exercise
Ashraf et al. (2005)[56]	5	1	1	1: 7% (5 of 70)	0	1	No
Williams et al. (2005)[57]	5	1	1	1: none	1 (>80%)	1	No
Macan et al. (2006)[58]	4	1	1	1: 9% (5 of 53)	1	0	No
Gardner et al. (2007)[59]	4	1	1	1: none	1	1	Sandwiches were supplied
Sobenin et al. (2008)[60]	4	1	1	1: 19% (8 of 42)	0	1	No
Sobenin et al. (2010)[61]	4	1	1	1: 19% (10 of 51)	0	1	No
Han et al. (2011)[20]	4	1	1	1: 4% (2 of 46)	0	1	Vitamin supplements & functional foods prohibited

[a] Industry sponsor provided funding for trial, or author was employed by the sponsor. It cannot be excluded that the sponsor was involved in design, data collection, or analysis.
[b] Diet modification provided for information; not included in quality score.

META-ANALYSIS FOR TOTAL CHOLESTEROL

Meta-analysis of 37 trials revealed a significant cholesterol-lowering effect of garlic preparations compared with placebo (mean difference TC = −15.25 [95%CI: −20.72, −9.78] mg/dL; $I^2 = 77\%$; $P < 0.0001$) (Figure 2). The cholesterol-lowering treatment effect was more pronounced in trials of longer duration ($subgroup_{>8\ wks}$: mean difference TC = −17.20 [95%CI: −23.10, −11.30] mg/dL; $I^2 = 79\%$; $P < 0.0001$; $n = 31$), in trials of subjects with higher mean baseline TC levels ($subgroup_{TC\ \ baseline\ >200\ mg/dl}$: mean difference TC = −17.32 [95%CI: −23.48, −11.16]; $I^2 = 81\%$; $P < 0.0001$; $n = 29$) (Figure 3), and in the subgroup of non-industry-sponsored trials ($subgroup_{nonsponsored}$: mean difference TC = − 18.30 [95%CI: −24.94, −11.66]; $I^2 = 77\%$; $P < 0.0001$; $n = 25$) (Table 4, section A).

Further comparison of trials of longer duration revealed a larger effect size in trials of 13–52 weeks in duration ($subgroup_{>12\ weeks}$: mean difference TC = − 19.63 [95%CI: −28.48, −11.30] mg/dL; $I^2 = 79\%$; $P < 0.0001$; $n = 14$) than in trials of 8–12 weeks in duration ($n = 17$) (Table 4, section A).

In contrast, subgroup analysis of trials of shorter duration (2–8 weeks, $n = 6$)[20,26,28,29,37,57] or trials of subjects with normal mean baseline TC levels (≤200 mg/dL, $n = 8$)[20,23,26,37,49,51,54,57,58] revealed no significant effect of garlic compared with placebo (Figure 3).

The majority of trials used garlic powder preparations ($n = 24$), although some used garlic oil ($n = 6$), aged garlic extract ($n = 5$), or raw garlic ($n = 2$). Subgroup analysis by single type of garlic preparation suggested a greater cholesterol-lowering effect for aged garlic extract than for garlic powder, and a borderline effect for garlic oil, while subgroup analysis with two studies using raw garlic is less meaningful (Table 4, section A). As enteric coating of garlic powder tablets may influence the bioavailability and effectiveness of garlic,[86] a sensitivity

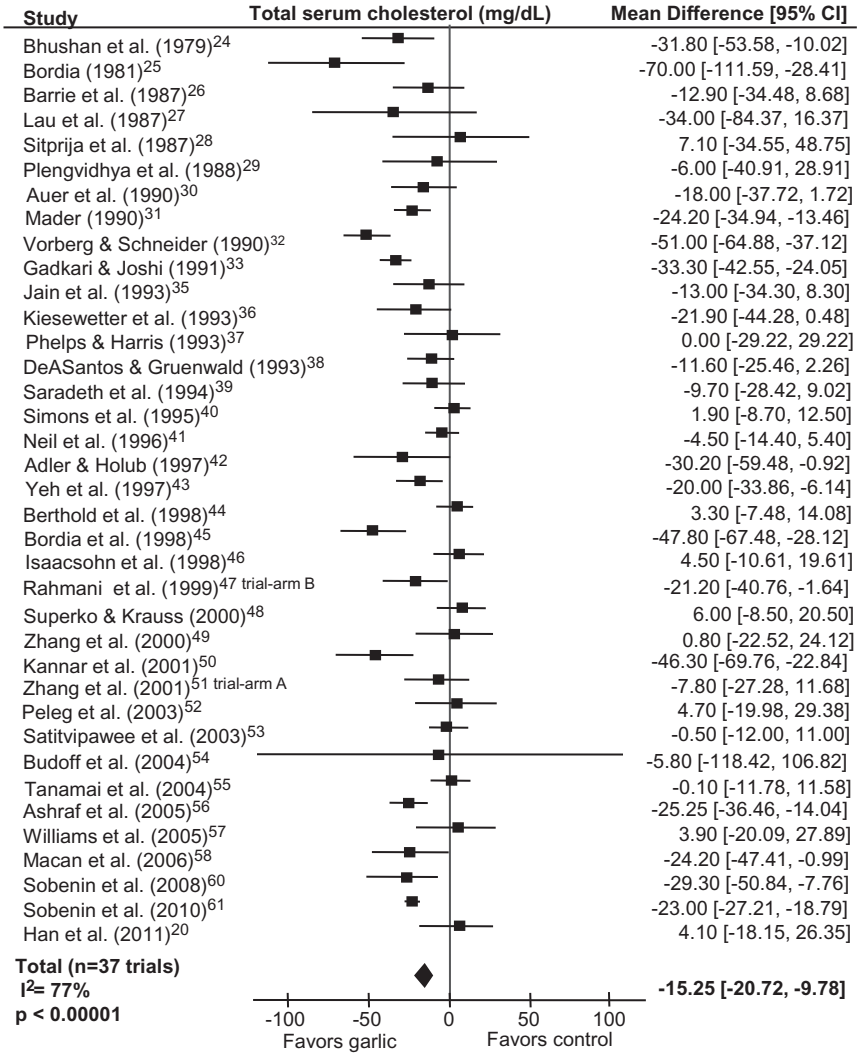

Figure 2 **Meta-analysis of trials testing the effect of garlic on total serum cholesterol.**

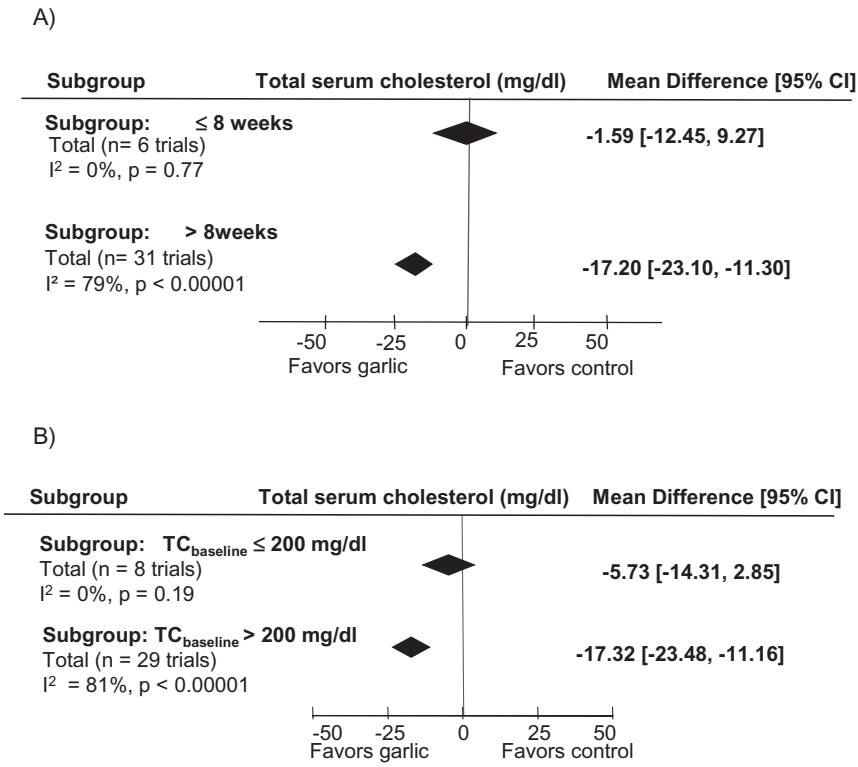

Figure 3 **Subgroup meta-analyses of the effect of garlic on total serum cholesterol by duration (A) and by mean total cholesterol (TC) level at baseline (B).**

analysis of trials using enteric-coated garlic powder tablets ($n = 18$) was conducted, resulting in a slightly larger effect than of all trials using any type of garlic powder ($n = 24$) (Table 4, section A).

Sensitivity analysis of trials using enteric-coated garlic powder tablets, garlic oil, aged garlic extract, or raw garlic were of longer duration (>8 weeks) and included subjects with mean baseline TC levels of at least 200 mg/dL, suggesting a mean difference of TC = − 18.28 mg/dL ($n = 18$) (Table 4, section B).

Additionally, sensitivity analysis using alternative active study arms[47,51] compared with placebo did not change results appreciatively, nor did sensitivity analysis excluding trials of low quality or with >20% attrition[33,41,51] or excluding trials that included participants on lipid-lowering medication (Table 3 and Table 4, section B).[31,54,57]

Meta-analysis for LDL cholesterol

Twenty-six trials reported the effect of garlic on LDL cholesterol levels. Meta-analysis including all trials showed a moderate significant reduction of LDL cholesterol by garlic compared with placebo (mean difference LDL = − 6.41 [95%CI: −11.77, −1.05] mg/dL, $I^2 = 75\%$; $P = 0.02$; $n = 26$) (Figure 4). The effect was larger in trials of longer duration ($subgroup_{>8wks}$: mean difference LDL = −7.17 [95%CI: −12.87, −1.47] mg/dL, $I^2 = 77\%$; $P = 0.01$; $n = 23$), in trials of subjects with higher mean baseline TC levels ($subgroup_{LDL\ baseline > 130\ mg/dl}$: mean difference LDL = −9.05 [95%CI: −15.19, −2.91] mg/dL, $I^2 = 78\%$; $P = 0.0004$; $n = 18$), and in non-industry-sponsored trials ($subgroup\ LDL_{nonsponsored}$: mean difference LDL = −8.21 [95%CI: −15.97, −0.44] mg/dL, $I^2 = 82\%$; $P = 0.04$; $n = 14$) (Table 4, section A).

Subgroup analysis by effect of garlic type on LDL cholesterol was significant for garlic powder. Only five trials investigated the effect of aged garlic extract on LDL; results are likely confounded by LDL baseline levels, as four of the five trials involved participants with LDL cholesterol levels of less than 130 mg/dL at baseline. Four trials tested the effect of garlic oil on LDL cholesterol levels, but two of these four trials involved subjects with normal LDL levels at baseline (Table 4, section A).

Sensitivity analysis that excluded trials using non-enteric-coated garlic powder tablets, trials designed with alternate active trial arms, trials of low quality, or trials with participants on lipid-lowering prescription medication did not change results for LDL cholesterol appreciably (Table 4, section B).

Table 4 **Subgroup analyses (A) and sensitivity analyses (B) of trials included in the meta-analysis.**

Trial type and characteristics		No. of trials	Effect size	95% CI	I^2 (%)	*P* value
A. Subgroup analyses						
TC (mg/dL)						
All trials		37	−15.25	−20.72, −9.78	77	<0.0001*
Type of garlic						
	GP	24	−13.19	−19.61, −6.77	78	<0.0001*
	GP_{ec}	18	−13.59	−20.93, −6.25	82	0.0003*
	AGE	5	−16.84	−27.22, −6.45	0	0.001*
	GO	6	−18.91	−38.65, 0.83	83	0.06
	RG	2	−33.07	−41.59, −24.56	0	<0.0001*
Duration of trial						
	≤8 wks	6	−1.59	−12.45, 9.27	0	0.77
	>8 wks (8–52 wks)	31	−17.2	−23.10, −11.30	79	<0.0001*
	8–12 wks	17	−15.47	−23.71, −7.24	78	0.0002*
	13–52 wks	14	−19.63	−28.48, −10.79	80	<0.0001*
Mean baseline TC						
	≤200 mg/dl	8	−5.73	−14.31, 2.85	0	0.19
	>200 mg/dl	29	−17.32	−23.48, −11.16	81	<0.0001*
Industry funding						
	Yes	12	−8.53	−16.00. −1.05	57	0.03*
	No	25	−18.30	−24.94, −11.66	77	<0.0001*
LDL cholesterol (mg/dL)						
All trials		26	−6.41	−11.77, −1.05	75	0.02*
Type of garlic						
	GP	19	−6.97	−13.55, −0.39	80	0.04*
	GP_{ec}	15	−5.82	−13.30, 1.67	82	0.13
	AGE	5[a]	−0.01	−10.97, 10.95	41	1.00
	GO	4[b]	−4.26	−11.48, 2.95	14	0.25
	RG	1	6	−2.86, 14.86	ne	ne
Duration of trial						
	≤8 wks	3	1.41	−11.35, 14.17	0	0.83
	>8 wks (8–52 wks)	23	−7.17	−12.87, −1.47	77	0.01*
Mean baseline LDL						
	≤130 mg/dL	8	3.51	−2.57, 9.59	0	0.26
	>130 mg/dL	17	−9.05	−15.19, −2.91	78	0.0004*
Industry funding						
	Yes	12	−2.01	−6.38, 2.35	0	0.37
	No	14	−8.21	−15.97, −0.44	82	0.04*
B. Sensitivity analyses						
TC, LDL cholesterol, HDL cholesterol, TG (mg/dL)						
Excluding trials of low quality and with high loss to follow-up: Gadkari & Joshi (1991),[33] Neil et al. (1996),[41] Zhang et al. (2001)[51]	TC	34	−15.17	−20.99, 9.36	76	<0.0001*
	LDL cholesterol	24	−6.78	−12.52, −1.03	76	0.02*
	HDL cholesterol	28	1.54	0.12, 2.95	38	0.03*
	TG	30	−4.73	−13.93, 4.47	72	0.31
Excluding trials involving patients on lipid-lowering medication: Mader (1990),[31] Budoff et al. (2004),[54] Williams et al. (2005)[57]	TC	34	−15.42	−21.15, −9.68	78	<0.0001*
	LDL cholesterol	24	−6.73	−12.23, −1.24	77	0.02*
	HDL cholesterol	28	1.51	0.16, 2.86	38	0.03*
	TG	29	−4.55	−13.60, 4.50	71	0.32

Table 4 **Continued**

Trial type and characteristics		No. of trials	Effect size	95% CI	I^2 (%)	*P* value
TC (mg/dL)						
All trials		37	−15.25	−20.72, −9.78	77	<0.0001*
Alternative active arms						
Rahmani et al. (1999)[47] with 3 trial-arms A,B,C	Not 2,400 mg/day GP (B) but 1,200 mg/day GP (A)	37	−14.83	−20.32, −9.33	77	<0.0001*
Rahmani et al. (1999)[47] with 3 trial-arms A,B,C	Not 2,400 mg/day GP (B) but 3,600 mg/day GP (C)	37	−14.75	−20.24, −9.26	77	<0.0001*
Zhang et al. (2001)[51] With 2 trial-arms A,B	Not GO (A) but GP (B)	37	−14.58	−20.09, −9.07	77	<0.0001*
LDL cholesterol (mg/dL)						
All trials		26	−6.41	−11.77, −1.05	75	0.02*
Alternative active arms						
Rahmani et al. (1999)[47] with 3 trial-arms A,B,C	Not 2,400 mg/day GP (B) but 1,200 mg/day GP (A)	26	−5.74	−11.16, −0.32	76	0.04*
Rahmani et al. (1999)[47] with 3 trial-arms A,B,C	Not 2,400 mg/day GP (B) but 3,600 mg/day GP (C)	26	−5.75	−11.15, −0.35	76	0.04*
Zhang et al. (2001)[51] with 2 trial-arms A,B	Not GO (A) but GP (B)	26	−6.34	−11.70, −0.98	75	0.02*
Gardner et al. (2007)[59] with 3 trial-arms A,B,C	Not AGE (C) but RG (A)	26	−6.46	−11.78, −1.13	75	0.02*
Gardner et al. (2007)[59] with 3 trial-arms A,B,C	Not AGE (C) but GP (B)	26	−6.33	−11.74, −0.92	75	0.02*
TC (mg/dL)						
Combination by type of garlic, duration of trial, and mean baseline TC levels	GP_{ec}/GO/AGE/RG, >8 wks, $TC_{baseline}$ >200 mg/dL	18	−18.28	−25.13, −11.44	83	<0.0001*

* Statistically significant $P < 0.05$.

[a] Four of the five trials investigating the effect of AGE on LDL cholesterol involved participants with a mean LDL of <130 mg/dL.

[b] Two of the four trials investigating the effect of GP on LDL cholesterol involved participants with a mean LDL of <130 mg/dL.

Abbreviations: AGE, aged garlic extract; GO, garlic oil; GP, garlic powder; GP_{ec}, enteric-coated garlic powder; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ne, not estimable; RG, raw garlic; TC, total cholesterol; TG; triglycerides.

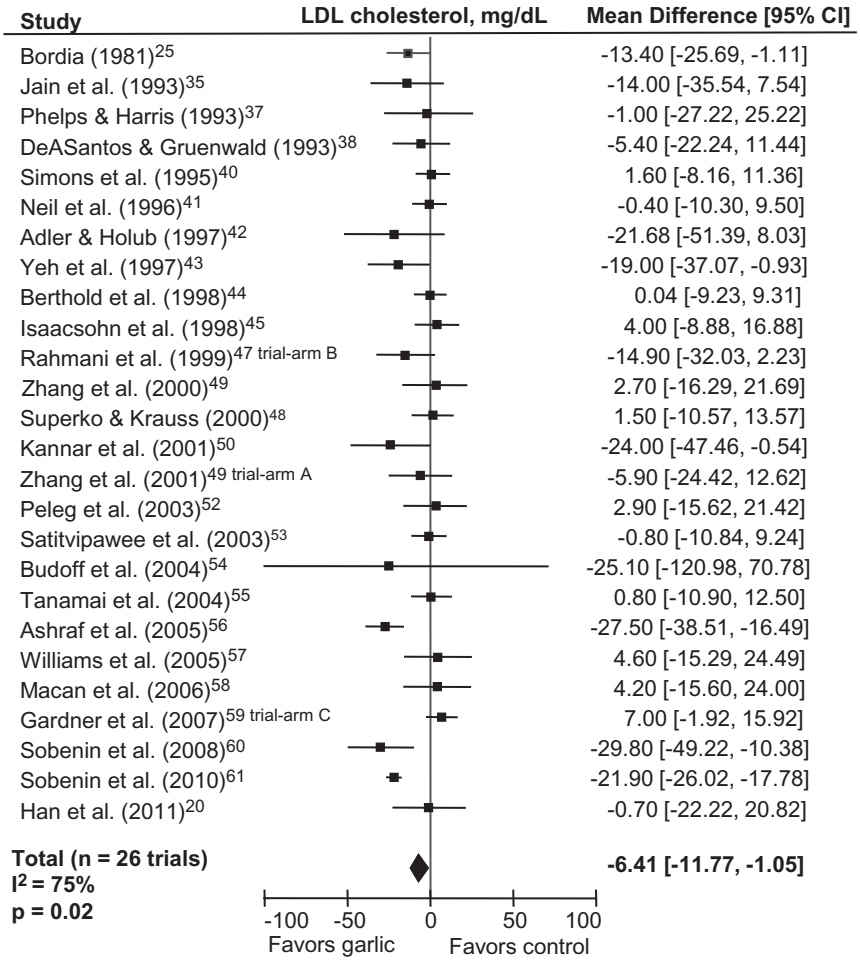

Figure 4 **Meta-analysis of trials testing the effect of garlic on low-density lipoprotein (LDL) cholesterol.**

Meta-analysis for HDL cholesterol and triglycerides

Meta-analysis of 30 trials on the effect of garlic on HDL cholesterol levels was significant but small (mean difference HDL = 1.49 [95%CI: 0.19, 2.79] mg/dL, $I^2 = 33\%$; $P = 0.02$) (Figure 5). Subgroup analysis of trials using garlic oil revealed the largest and statistically significant effect (mean difference $HDL_{garlic\ oil} = 5.97$ [95%CI: 1.65, 10.30] mg/dL, $I^2 = 67\%$; $P = 0.007$, $n = 6$), whereas results of subgroup analysis of trials investigating other types of garlic were not significant.

The effect of garlic on triglycerides levels was reported by 32 trials but did not reveal a significant effect (mean difference triglycerides = −5.45 [95%CI: −14.18, 3.27] mg/dL, $I^2 = 71\%$; $P = 0.22$) (Figure 6).

Additional subgroup and sensitivity analyses did not change results for HDL cholesterol or triglycerides appreciably (data not shown).

Side effects

Twenty-three of the 39 trials (60%) reported on side effects (Table 5). Garlic odor, breath, or taste was noticed in a greater proportion of participants in the active treatment group in 13 trials using garlic powder or raw garlic (mean = 30%) compared with placebo (mean = 10%).

Fifteen trials reported gastrointestinal side effects in a small number of participants in the active treatment groups (7%), but the number was not appreciably different from that in placebo groups (7%), while eight trials stated no gastrointestinal complaints of participants. Gastrointestinal side effects included mild discomfort, flatulence, bloating, reflux, and belching. Reported side effects were not associated with the type of garlic preparation or dosage.

Three trials[28,40,58] investigated the effect on liver biomarkers and hematology. All reported no changes in liver function, biochemistry, or hematology. One trial with patients on warfarin therapy (mean age, 56 ± 10 years) found no differences in bleeding abnormalities or other adverse interactions between aged garlic extract and warfarin.[58]

Publication bias

Funnel plots using Begg's test of trials to investigate the effect of garlic on cholesterol (TC, LDL, HDL)

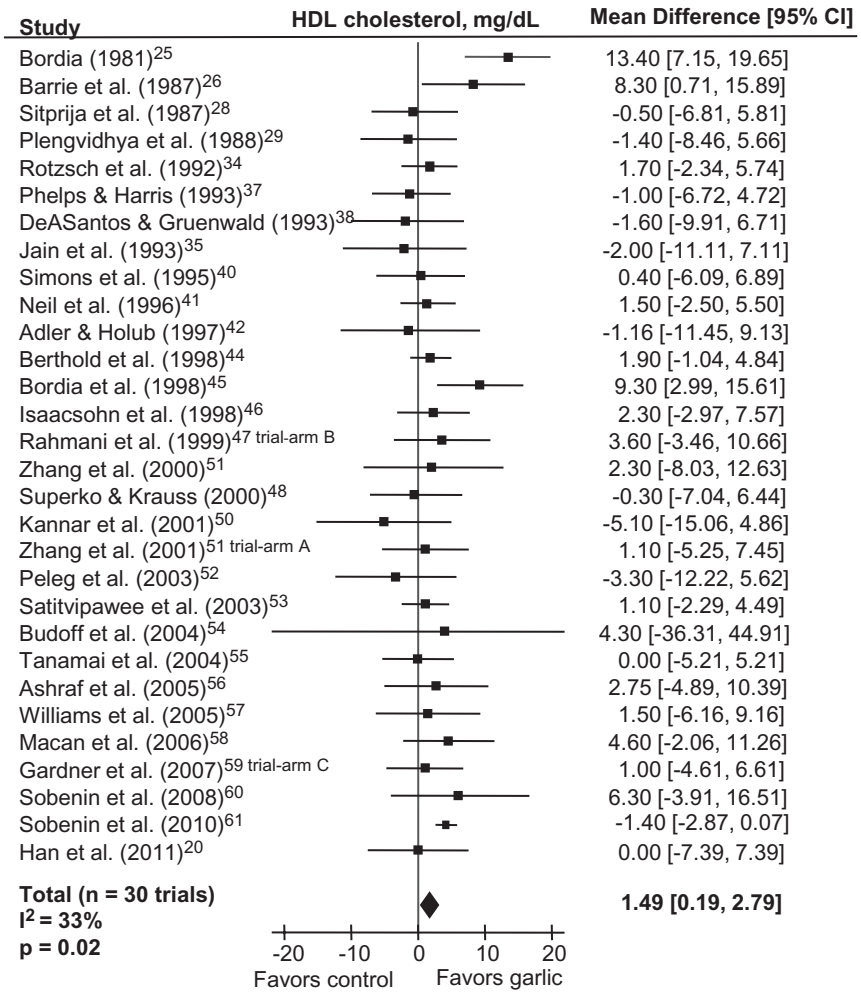

Figure 5 **Meta-analysis of trials testing the effect of garlic on high-density lipoprotein (HDL) cholesterol.**

and triglyceride levels indicated no publication bias (Figure 7).

Comparison with previous published meta-analyses

The effect of garlic preparations on lipid parameters has been studied previously by others, but providing conflicting conclusions.[13–19] While early meta-analyses by Warshafsky et al.[13] and Silagy and Neil[14] reported a statistically significant and clinically relevant lowering effect of garlic on total serum cholesterol, the next set of meta-analyses by Stevinson et al.,[15] Ackermann et al.,[16] and Khoo and Aziz[17] questioned the robustness of such findings as well as the reported clinical effectiveness. More recent meta-analyses by Reinhart et al.[18] and Zeng et al.,[19] which included a larger number of trials, reported a larger clinically modest effect of garlic on lipid parameters. The present meta-analysis includes 39 trials, which is the largest set of trials included to date, and incorporates trials reported in early meta-analyses[13,14] as well as more recent trials (Table 6).

In contrast to the meta-analyses by Zeng et al.,[19] this meta-analysis included each trial only once in the analysis if the trial studied multiple intervention arms compared with one control arm (3 active arms[59] and 2 active arms[51]); this was done to avoid bias. In contrast to the meta-analysis by Reinhart et al.,[18] this meta-analysis included only the first phase of a crossover trial if there was no washout between treatments.[29,55]

Furthermore, mean differences between treatment groups at the end of each trial were adjusted by mean baseline values. These adjustments were particularly influential when baseline values differed greatly between the intervention and control groups. For example, in Zhang et al.,[51] the mean baseline level for TC for the garlic/control groups (n = 20/21) was 166.4/189.6 mg/dL, and the mean TC at the end of the trial for the garlic/control groups was 162.9/187.9 mg/dL, resulting in a mean difference (between garlic and control at follow-up) of −25 mg/dL without adjustment and of −1.8 mg/dL with adjustment by baseline (Table 1). While randomization of treatment and control groups aims for comparable

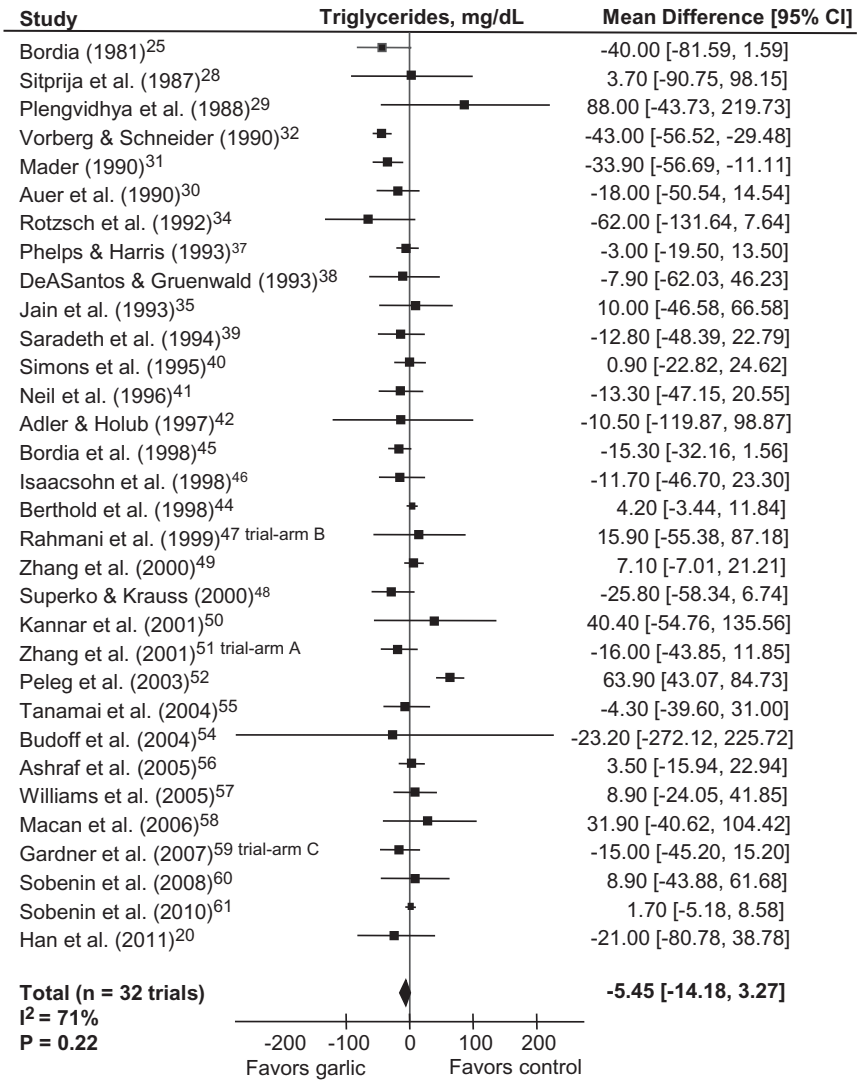

Figure 6 **Meta-analysis of trials testing the effect of garlic on triglycerides.**

baseline characteristics, this might not be achieved in smaller trials.

DISCUSSION

This meta-analysis on the effect of garlic on cholesterol suggests garlic to be effective in reducing total serum cholesterol by 17 ± 6 mg/dL and LDL cholesterol by 9 ± 6 mg/dL in individuals with elevated total cholesterol levels (>200 mg/dl), provided garlic is taken for more than 2 months. HDL cholesterol levels improved slightly, by 1.5 ± 1.3 mg/dL, and triglycerides levels were not influenced significantly. These results were strengthened in subgroup analyses that included only non-industry-sponsored trials.

While the reductions in total serum cholesterol and LDL cholesterol were modest in comparison with those obtained with standard cholesterol-lowering medication (e.g., statins), garlic preparations were highly tolerable and were associated with minimal side effects and with none of the serious adverse effects that may be elicited by standard drug treatment in a considerable number of patients.[4,5] Furthermore, the observed 8% reduction in total serum cholesterol with garlic in subjects with elevated cholesterol (mean TC>212 mg/dL or 5.5 mmol/L) is of clinical relevance and is associated with a 38% reduction in risk of coronary events at age 50.[1,2] The strength of the association between cholesterol and coronary risk reduction is also influenced by other cardiovascular risk factors, including blood pressure and age.[3] Similarly, the 9% reduction in LDL cholesterol levels, while modest, may contribute to a 6% reduction in risk of adverse coronary and vascular events.[87]

The cholesterol-lowering properties of garlic have been linked to the inhibition of cholesterol synthesis[88,89] and the suppression of LDL oxidation.[90] A variety of

Table 5 **Side effects reported in trials included in the meta-analysis.**

Reference	Garlic type	Garlic odor		Gastrointestinal side effects		Details of gastrointestinal side effects[a]
		Garlic group, % (*n*)	Control group, % (*n*)	Garlic group, % (*n*)	Control group, % (*n*)	
Bhushan et al. (1979)[24]	RG	NR	NR	NR	NR	
Bordia (1981)[25]	GO	None	None	12% (4 of 33)	None	G: discomfort (*n* = 3), diarrhea (*n* = 1)
Barrie et al. (1987)[26]	GO	NR	NR	NR	NR	
Lau et al. (1987)[27]	AGE	None	None	6% (1 of 15)	None	G: flatulence (*n* = 1)
Sitprija et al. (1987)[28]	GP	None	None	None	None	
Plengvidhya et al. (1988)[29]	GP	NR	NR	NR	NR	
Auer et al. (1990)[30]	GP	13% (3 of 24)	None	None	None	
Mader (1990)[31]	GP	19% (21 of 111)	7% (8 of 112)	1% (1 of 111)	3% (3 of 112)	G&P: minor GI discomfort (*n* = 1/*n* = 3); P: allergic reaction (*n* = 1)
Vorberg & Schneider (1990)[32]	GP	NR	NR	NR	NR	
Gadkari & Joshi (1991)[33]	RG	None	None	None	None	
Rotzsch et al. (1992)[34]	GP	NR	NR	NR	NR	
Jain et al. (1993)[35]	GP	None	None	4% (1 of 20)	18% (4 of 22)	G: belching (*n* = 1); P: mild discomfort (n = 2), prolonged bleeding by razor cut (*n* = 1), minor rash (*n* = 1)
Kiesewetter et al. (1993)[36]	GP	28% (9 or 32)	13% (4 of 32)	None	None	
Phelps & Harris (1993)[37]	GP	NR	NR	NR	NR	
DeA Santos & Gruenwald (1993)[38]	GP	None	None	4% (1 of 25)	None	G: flatulence (*n* = 1)
Saradeth et al. (1994)[39]	GP	NR	NR	NR	NR	
Simons et al. (1995)[40]	GP	43% (12 of 28)	None	11% (4 of 28)	7% (2 of 28)	G&P: bloating, nausea, flatulence (*n* = 4/*n* = 2)
Neil et al. (1996)[41]	GP	33% (19 of 57)	9% (5 of 58)	None	None	G: discomfort (*n* = 12)
Adler & Holub (1997)[42]	GP	17% (2 of 12)	None	None	None	
Yeh et al. (1997)[43]	AGE	13% (2 of 16)	None	6% (1 of 16)	none	G: reflux (*n* = 1)
Berthold et al. (1998)[44]	GO	Few cases	Few cases	Few cases	Few cases	G: mild discomfort
Bordia et al. (1998)[45]	GO	NR	NR	NR	NR	
Isaacsohn et al. (1998)[46]	GP	11% (3 of 28)	None	11% (3 of 28)	5% (1 of 22)	G: constipation (*n* = 1), discomfort (*n* = 2); P: reflux (*n* = 1)
Rahmani et al. (1999)[47]	GP	NR	NR	NR	NR	
Superko & Krauss (2000)[48]	GP	NR	NR	NR	NR	
Zhang et al. (2000)[49]	GO	NR	NR	NR	NR	
Kannar et al. (2001)[50]	GP	90% (18 of 20)	None	Few cases	Few cases	G: reflux (n = 1), G&P: increased bowel movement, flatulence, bloating
Zhang et al. (2001)[51]	GO	NR	NR	NR	NR	
Peleg et al. (2003)[52]	GP	NR	NR	Few cases	Few cases	
Satitvipawee et al. (2003)[53]	GP	NR	NR	Few cases	Few cases	G&P: belching, bloating, nausea, constipation
Budoff et al. (2004)[54]	AGE	NR	NR	NR	NR	
Tanamai et al. (2004)[55]	GP	Few cases	None	4% (2 of 45)	None	G: itching (*n* = 1), headache (*n* = 1)
Ashraf et al. (2005)[56]	GP	NR	NR	3% (1 of 35)	None	G: reflux
Williams et al. (2005)[57]	AGE	NR	NR	NR	NR	
Macan et al. (2006)[58]	AGE	NR	NR	None	None	
Gardner et al. (2007)[59]; trial arm A	RG	57% (28 of 49)	None	7% (3 of 42)	2% (1 of 43)	G&P: flatulence
Gardner et al. (2007)[59]; trial arm B	GP	None	None	10% (4 of 41)	As above	G&P: flatulence
Gardner et al. (2007)[59] trial-arm C	AGE	2% (1 of 42)	None	10% (4 of 42)	As above	G&P: flatulence
Sobenin et al. (2008)[60]	GP	None	None	None	None	
Sobenin et al. (2010)[61]	GP	NR	NR	NR	NR	
Han et al. (2011)[20]	GP	NR	NR	NR	NR	

Abbreviations: AGE, aged garlic extract; GO, garlic oil; G, garlic group; G&P, garlic and placebo groups; GP, garlic powder; NR, not reported; P, placebo group; RG, raw garlic.

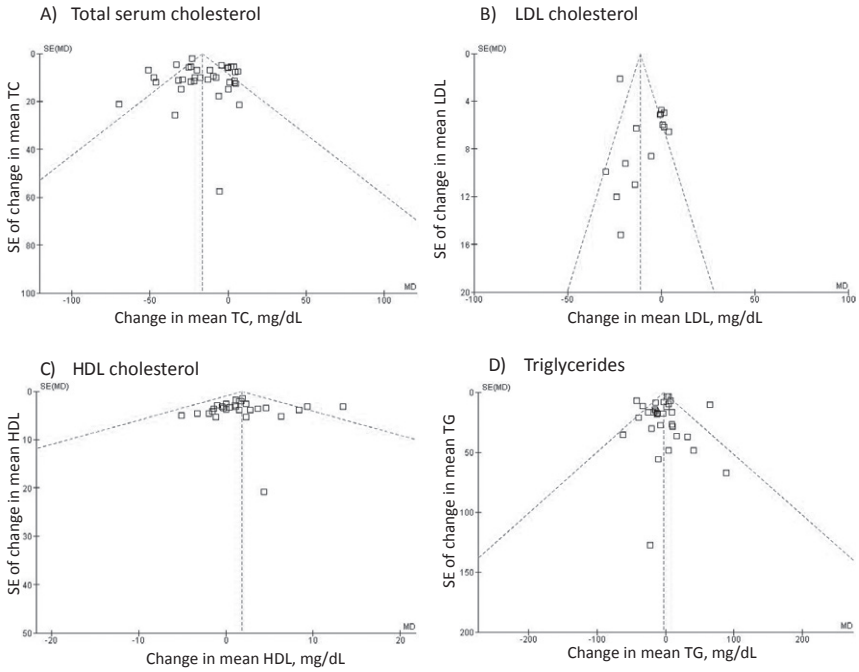

Figure 7 **Funnel plots of trials included in the meta-analysis on the effect of garlic on total serum cholesterol (A), low-density lipoprotein (LDL) cholesterol (B), high-density lipoprotein (HDL) cholesterol (C), and triglycerides (D).** *Abbreviations*: HDL, high-density lipoprotein; LDL, low-density lipoprotein; SE, standard error; TG, triglycerides; TC, total cholesterol.

organosulfur components in garlic preparations may, to different degrees, exert cardiovascular effects/benefits.

S-allylcysteine (commonly known by its abbreviation SAC) has been identified as the active and stable component in aged garlic extract, allowing standardization of preparations by S-allylcysteine dosage, but the active component in garlic powder is less well established, as the commonly named allicin, an alliin derivate, is volatile and is likely only transiently responsible for the cardiovascular effects.[91,92]

Furthermore, the bioavailability of active compounds in garlic powder tablets has been shown to be affected by preparation and design; e.g., Kwai® garlic powder tablets made before 1993 were enteric coated with calcium-carbonate and resulted in better bioavailability and effectiveness than Kwai® garlic powder tablets without enteric coating produced after 1993.[86] In addition, allicin release of garlic powder tablets is dependent on the activity of the enzyme alliinase and the quality of the garlic powder.[93]

In the present meta-analysis, subgroup meta-analysis by type of garlic preparation suggests aged garlic extract to be more effective than garlic powder or garlic oil in reducing total serum cholesterol. In addition, effect sizes increased if trials using non-enteric-coated garlic powder

Table 6 **Results of meta-analyses on the effect of garlic on lipid parameters.**

Reference	No. of trials in meta-analysis	Mean difference (SE) between garlic and control group (mg/dL)			
		Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
Warshafsky et al. (1993)[13]	6	−23.0 (6.0)	NR	NR	
Silagy & Neil (1994)[14]	14	−29.8 (4.6)	NR	−1.6 (0.4)	27.5 (15.9)
Stevinson et al. (2000)[15]	13	−15.7 (10.0)	−6.6 (6.2)	2.7 (1.2)	NR
Ackermann et al. (2001)[16]	33[a]	−7.2 (6.0)	6.2 (5.4)	0.9 (1.8)	−19.1 (10.6)
Khoo & Aziz (2009)[17]	12	−1.6 (4.3)	0.4 (3.9)	0.4 (1.6)	−4.4 (10.6)
Reinhart et al. (2009)[18]	29	−7.4 (5.4)	2.3 (3.6)	1.0 (0.9)	−9.8 (7.1)
Zeng et al. (2012)[19]	26	−10.8 (6.6)	0 (2.7)	0.4 (0.4)	−11.5 (6.2)
Ried et al. (2013)[present review]	39	−15.2 (5.5)	−6.4 (5.4)	1.8 (1.2)	−5.5 (8.7)

[a] Ackermann et al.[16] included a total of 43 trials in the systematic review but included six trials that did not use a placebo control group and four trials that used a garlic combination product. The remaining 33 trials are comparable to the number of trials included in the other meta-analyses.
Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; NR; not reported; SE, standard error.

were excluded. Garlic powder seemed to be more effective for reducing LDL cholesterol, while garlic oil appeared to be more effective for increasing HDL cholesterol. However, subgroup analyses by garlic type need to be interpreted cautiously, as subgroups with only a small number of trials using aged garlic extract or garlic oil are likely confounded by lipoprotein levels of participants at baseline. Comparison by dosage was not meaningful, as not all trials established or reported the dosage of active ingredients.

This review found garlic preparations to be highly tolerable. While one-third of the population may have noticed a characteristic garlic odor, taste, or breath, mild gastrointestinal side effects were experienced by a small proportion of the population (7%) and included flatulence, bloating, belching, and reflux. However, these gastrointestinal complaints were also reported by a similar proportion of participants in the placebo groups, indicating that gastrointestinal effects may not be solely attributable to garlic preparations and may be influenced by other dietary and lifestyle factors.

Despite the general medical advice, evidence is weak for garlic to cause harmful interactions if taken in addition to blood-thinning, blood-sugar-regulating, or anti-inflammatory medications.[94] Physicians and patients need to be mindful, however, of a potentially harmful interaction of garlic with protease inhibitors in antiretroviral therapy.[94]

In comparison, standard drug therapy with statins can elicit more debilitating and sometimes serious side effects in some patients, including muscular pain, sexual dysfunction, cognitive impairment, increased risk of diabetes, and mood disorders that include aggressive behavior, anxiety, and irritability.[6–10,95,96]

Cholesterol is essential for normal body functions that include preserving the integrity of cell membranes, facilitating cell signalling, maintaining the myelin sheath, and synthesizing steroid hormones, vitamin D, and coenzyme Q10. Inhibition of cholesterol synthesis by statin drugs may interfere with these essential pathways, resulting in detrimental effects for some patients.[9,10,95]

This systematic review, the most comprehensive to date, includes the largest number of trials ($n = 39$) investigating the effect of garlic preparations on blood lipids, thereby allowing for meaningful subgroup analyses by trial duration, baseline cholesterol levels, and type of garlic preparation. This review also includes a sensitivity analysis, which allows comparison of the effects of different active treatment arms versus placebo of three trials[47,51,59] rather than including all comparisons between different active treatment arms and the same placebo group,[19] which would have introduced bias. In addition, for the first time, reported side effects in included trials are summarized, and more detail on dosages is provided.

Certain limitations of this review should be noted. Due to high heterogeneity in meta-analyses, resulting effect sizes should be interpreted with some caution. Reasons for heterogeneity can only partly be explained by variables explored in subgroup analysis. While trials of shorter duration or with lower baseline cholesterol levels were more homogeneous, subgroup analysis of trials of longer duration or with higher baseline cholesterol levels remained highly heterogeneous, implying the presence of additional factors that may explain the high variability between studies. Available data were insufficient to undertake subgroup analysis by dosage of active ingredient, a likely confounding factor.

CONCLUSION

This updated meta-analysis suggests garlic to be superior to placebo for reducing elevated total serum cholesterol on a clinically significant level. Garlic has been shown to have additional cardiovascular benefits, such as lowering blood pressure in hypertensives,[97–99] increasing fibrinolytic activity, and reducing platelet aggregation.[11] Taken together, garlic preparations may be viewed as a general heart and cardiovascular tonic with cholesterol-regulating properties and might be considered as an alternative option with a higher safety profile than conventional cholesterol-lowering medications for patients with slightly elevated cholesterol. Future trials on the effect of garlic on blood lipids should include information on the dosage of active ingredients of standardized garlic preparations for better comparison of trials.

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