Garlic for treating hypercholesterolemia: a meta-analysis of randomized clinical trials

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Authors' objectives
To investigate the effect of garlic on total cholesterol level in persons with elevated levels.

Searching
MEDLINE, EMBASE, BIOSIS Previews, AMED, the Cochrane Library and CISCOM databases were searched from inception to November 1998 using search terms 'garlic', 'Allium sativum' and 'Knoblauch'. Manufacturers of garlic preparations and experts in the field were asked about published or unpublished trials, and the bibliographies of retrieved papers were scanned. There were no language restrictions.

Study selection
Study designs of evaluations included in the review
Randomised double-blind placebo-controlled trials which reported total cholesterol level as an end point.

Specific interventions included in the review
Garlic monopreparations (essential oil, spray-dried powder, standardised powder (Kwai), steam-distilled oil) at daily doses of 10mg, 0.25mg/kg body mass, or 540-7200mg, for a duration of 4-24 weeks. All were compared to placebo.

Participants included in the review
Persons with mean total cholesterol levels of at least 5.17 mmol/L (200mg/dL). Participants had diagnoses which included coronary heart disease, hyperlipoproteinemia, hypercholesterolemia, 'normal', familial hyperlipidemia in children, thrombocyte aggregation.

Outcomes assessed in the review
Total cholesterol level was the primary outcome measure. The authors also report triglyceride, high-density lipoprotein (HDL) and low density lipoprotein (LDL) cholesterol levels where these are reported in the included studies.

How were decisions on the relevance of primary studies made?
Two of the authors evaluated methodologic quality independently and discrepancies were resolved through discussion.

Assessment of study quality
Methodologic quality was assessed by the Jadad scale (see Other Publications of Related Interest no.1). Two of the authors evaluated methodologic quality independently and discrepancies were resolved through discussion.

Data extraction
Two of the authors extracted data independently and discrepancies were resolved through discussion. Data were extracted in a systematic manner according to predefined criteria. Where information was insufficient for statistical pooling, the authors of the study and manufacturers were approached in an attempt to obtain more details. Data were extracted on: study design, participant diagnosis, baseline lipid levels, number of participants randomised, number of participants analysed, type of garlic extract, dose, duration of intervention, control of lifestyle factors, and results. Where studies did not report enough information to calculate variance of change in total cholesterol levels, an assumption of a correlation of 0.4 between pre-intervention and post-intervention values was used to impute the variance of the change (see Other Publications of Related Interest no.2).

Methods of synthesis
How were the studies combined?
Weighted means (of changes in total cholesterol level compared with baseline) and 95% confidence intervals (CIs) were
calculated using a random-effects model. Publication bias was assessed by using a funnel plot (see Other Publications of Related Interest no.3).

How were differences between studies investigated?
The chi-squared test for homogeneity was performed. Two sensitivity analyses were conducted. The first included only five trials using the same standardised garlic preparation. The second included only six trials with the highest Jadad quality scores.

Results of the review
Thirteen randomised controlled trials (n=796) were included in the meta-analysis. Five other trials which met the inclusion criteria but did not report enough data to be included in the meta-analysis included 232 participants.

All trials except one (which scored 2) scored between 3 and 5 points on the Jadad quality scale.

Garlic reduced total cholesterol level from baseline significantly more than placebo (p<0.01) weighted mean difference (WMD) -0.41mmol/L (95% CI: -0.66, -0.15 mmol/L) or -15.7mg/dL (95% CI: -25.6, -5.7 mg/dL). Significant heterogeneity was found on a chi-square test (chi-square = 36.76). When one trial with an outlying result was removed the results were homogeneous and WMD was -0.30mmol/L (95% CI: -0.48, 0.11 mmol/L) or -11.4mg/dL (95% CI: -18.6, -4.2 mg/dL).

The results of the two sensitivity analyses showed no significant differences between the groups.

Five trials reported data on HDL and LDL cholesterol levels; no significant differences between groups were found.

Adverse events (10 RCTs): the most frequently reported adverse events were gastrointestinal symptoms and garlic breath.

There was no evidence of publication bias (symmetry of the funnel plot was confirmed by a regression test of all trials).

Of five trials which did not provide enough data to be included in the meta-analysis, four showed no significant difference between garlic and placebo and one (with the highest daily dose of 7200mg) showed a difference in favour of garlic.

Authors' conclusions
The available data suggest that garlic is superior to placebo in reducing cholesterol levels. However, the size of the effect is modest, and the robustness of the effect is debatable. The use of garlic for hypercholesterolemia is therefore of questionable value.

CRD commentary
This is, on the whole, a methodologically sound review which is well reported. The review question was clearly stated and well supported by study inclusion criteria. The literature search was comprehensive and efforts were made to find unpublished studies. There were stated to be no language restrictions, although only English and German search terms were used. Validity assessment was performed using a validated scale and results were presented appropriately. Study details were well reported and pooling seemed appropriate. Heterogeneity was assessed, although reasons for heterogeneity were not explored. Some details of review methodology (i.e. how many reviewers extracted data etc) were reported but some were missing. Some studies were included which did not appear to meet the inclusion criteria, which may cast doubt on the validity of the results of the meta-analysis.

The authors’ conclusions do seem to follow from the results presented, but should be treated with some caution, given the limitations mentioned above.

Implications of the review for practice and research
Practice: The authors state that garlic use is not an efficient way to decrease total serum cholesterol level and that patients expressing interest in taking garlic for this reason should be advised that, according to current evidence, any specific effect is small and may not be clinically meaningful.

Research: The authors state that well-designed placebo-controlled trials comparing the efficacy of different types of garlic preparations at similar doses would help determine whether garlic has a specific effect on cholesterol levels and would provide clues to its active ingredients. They also state that large-scale long-term studies are needed to provide useful data on any association between garlic consumption and important clinical outcomes.

Bibliographic details

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http://www.annals.org/cgi/content/full/133/6/420

Other publications of related interest

This additional published commentary may also be of interest. Lawson LD. Garlic for total cholesterol reduction. Ann Intern Med 2001;135:65-6.

Indexing Status
Subject indexing assigned by NLM

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.