

## Review

# Clinical effectiveness of garlic (*Allium sativum*)

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The objective of this review is to update and assess the clinical evidence based on rigorous trials of the effectiveness of garlic (*A. sativum*). Systematic searches were carried out in Medline, Embase, Amed, the Cochrane Database of Systematic Reviews, Natural Standard, and the Natural Medicines Comprehensive Database (search date December 2006). Our own files, the bibliographies of relevant papers and the contents pages of all issues of the review journal FACT were searched for further studies. No language restrictions were imposed. To be included, trials were required to state that they were randomized and double blind. Systematic reviews and meta-analyses of garlic were included if based on the results of randomized, double-blind trials. The literature searches identified six relevant systematic reviews and meta-analysis and double-blind randomized trials (RCT) that were published subsequently. These relate to cancer, common cold, hypercholesterolemia, hypertension, peripheral arterial disease and pre-eclampsia. The evidence based on rigorous clinical trials of garlic is not convincing. For hypercholesterolemia, the reported effects are small and may therefore not be of clinical relevance. For reducing blood pressure, few studies are available and the reported effects are too small to be clinically meaningful. For all other conditions not enough data are available for clinical recommendations.

**Keywords:** Allium sativum / Alternative Medicine / Complementary Medicine / Garlic / Systematic review

Received: February 28, 2007; revised: May 8, 2007; accepted: May 11, 2007

## 1 Introduction

Garlic (*Allium sativum*) has been used as a food and spice in many countries for millennia. It has also been used in most cultures for various medicinal purposes [1]. However, its extensive scientific investigation started relatively recently. Today it is one of the best-researched and best-selling herbal remedies [2, 3]. Garlic has been used both orally and topically, most frequently for treating hypercholesterolemia and preventing arteriosclerosis, for preventing or treating infections and as a way of maintaining general health. Its best-researched property is that of lowering total serum cholesterol levels [4, 5].

The importance of allicin for the lipid lowering properties of garlic has been suggested by the results of a number of *in vivo* studies (e.g. [6]). The sulphur-containing compound alliin – the main ingredient of garlic – is broken

down by the enzyme alliinase and converted to allicin. This in turn is degraded into ajoene and polysulfides that are responsible for the distinctive smell of garlic. Commercial preparations of garlic are usually standardized to alliin content.

The body of evidence on garlic continues to grow and additional clinical trials have been published. The aim of this review is to update and assess the clinical evidence based on rigorous trials of the effectiveness of garlic (*A. sativum*).

## 2 Methods

Systematic searches were carried out in the databases Medline, Embase, Amed, the Cochrane Database of Systematic Reviews, Natural Standard, and the Natural Medicines Comprehensive Database. Each database was searched from its respective inception until December 2006. In addition, our own files, the bibliographies of relevant papers and the contents pages of all issues of the review journal FACT (Focus on Alternative and Complementary Therapies, Pharmaceutical Press, London, [www.pharmpress.com/fact](http://www.pharmpress.com/fact)) were searched for further studies. The search terms used were garlic, *Allium sativum*, and Knoblauch. No

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**Abbreviation:** RCT, randomized trials

language restrictions were imposed. Studies in languages other than English were translated in-house.

To be included, trials were required to state that they were randomized trials (RCT), conducted double blind and used garlic monoprparations. Systematic reviews and meta-analyses of garlic were included if based on the results of randomized, double-blind trials. Studies assessing short-term (*i.e.* within hours of administration) effects were excluded.

### 3 Results

The literature searches identified six relevant systematic reviews and meta-analyses and double-blind RCT that were published subsequently. These relate to cancer, common cold, hypercholesterolemia, hypertension, peripheral arterial disease and pre-eclampsia.

#### 3.1 Cancer

Epidemiologic data suggest that high intake of garlic is associated with a protective effect against stomach and colorectal cancers [7]. This is supported by two additional small double-blind RCT ( $n = 37, 50$ ) suggesting both preventative and therapeutic effects for colorectal adenoma formation and an increased number and activity of natural-killer cells [8, 9]. However, a large ( $n = 3365$ ) double blind RCT found that long-term garlic supplementation has no beneficial effects on the prevalence of precancerous gastric lesions or on gastric cancer incidence [10].

#### 3.2 Common cold

One double-blind RCT assessing 146 patients over a 12-week treatment period was identified [11]. Common cold infections and symptoms were recorded in a daily diary. Patients in the treatment group had significantly fewer colds than patients in the placebo group who had also a longer duration of symptoms.

#### 3.3 Hypercholesterolemia

RCT have tested the effects of garlic on total cholesterol and LDL levels. A meta-analysis of 13 double blind RCT reported a modest reduction of 15.7 mg/dL (95% CI 25.6 to 5.7 mg/dL) compared with placebo over a treatment period of 8 to 24 weeks [12], which was largely corroborated by an independent systematic review [13]. In an updated meta-analysis ( $n = 971$ ) including three additional trials, the effect was diminished to 13.6 mg/dL (95% CI 21.2 to 6.1 mg/dL) [14]. Four double-blind RCT ( $n = 3670$ ) were identified since this updated meta-analysis [15–18]. All reported no changes in lipid levels for hypercholesterolemic patients.

#### 3.4 Hypertension

A meta-analysis included ten double blind RCT that assessed blood pressure [19]. Overall, a significant reduction in systolic and diastolic blood pressure of 8 and 5 mmHg, respectively, was reported. When only hypertensive patients ( $n = 87$ ) were included, the analysis showed a significant reduction of 11 and 7 mmHg for systolic and diastolic blood pressure, respectively, compared with placebo. A more recent systematic review identified no further double blind placebo-controlled RCT [13]. Since then, another double-blind RCT ( $n = 85$ ) was published that reported a reduction of systolic and diastolic blood pressure in patients with mild to moderate hypertension [20].

#### 3.5 Peripheral arterial disease

A Cochrane review [21] of garlic extract for treating intermittent claudication identified one RCT [22], which was confirmed by an updated Cochrane literature search and an independent systematic review [23]. This 12-week double-blind, placebo-controlled trial included 78 patients. In addition to *A. sativum* extract, all patients received physical therapy twice weekly. No significant beneficial effects compared with placebo were reported.

#### 3.6 Pre-eclampsia and complications

Pre-eclampsia affects about 2 to 8% of pregnant women and is associated with hypertension and proteinuria. A Cochrane review [24] identified no double-blind RCT on the subject. It identified one single-blind RCT ( $n = 100$ ) [25] that showed not clear difference between garlic and placebo in the risk of developing gestational hypertension or pre-eclampsia. The review concludes that there is insufficient evidence to recommend garlic for preventing pre-eclampsia and its complications.

### 4 Discussion

The result of this systematic review suggests that there is no convincing evidence of effectiveness for garlic in any condition. Most trials have been conducted on hypercholesterolemia, suggesting small effects that may be of debatable clinical relevance. The most recent trial data suggest no effects on lipid levels. For hypertension, data from 172 patients are available, which suggest small effects on systolic and diastolic blood pressure. For all other conditions only single, if any, double-blind RCT were identified, which require independent replication.

Inefficiency and inconsistency in the *in vivo* production of allicin from the alliin contained in garlic preparations may explain some of the negative findings in rigorous clinical trials in hypercholesterolemic patients [26]. To what

extent these data can account for the negative results is uncertain. Other preparations have also yielded negative findings and the relevance of allicin for the lipid-lowering properties of garlic is not clear. Commercial preparations of garlic are usually standardised to alliin content, but the active ingredients and mechanism of action remain unknown.

Compared with conventional methods of lipid lowering, the reduction that may be achieved with garlic seems minimal at best. Following dietary advice, for example, total serum cholesterol is reduced by 0.13 mmol/L (95% CI 0.03 to 0.23) and LDL cholesterol by 0.13 mmol/L (95% CI 0.01 to 0.25) after 3–12 months compared with no advice [27]. Lipid lowering with 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors has dramatically reduced morbidity and mortality in patients with established cardiovascular disease. A review of the large-scale, randomized, placebo-controlled trials of high-dose statin therapy will soon become available [28]. Another systematic review of randomised clinical trials of statin drugs has reported a 12% proportional reduction in all-cause mortality per mmol/L reduction in LDL cholesterol and concluded that statin therapy can safely reduce the 5-year incidence of major coronary events and stroke by about one fifth per mmol/L reduction in LDL cholesterol [29].

Collectively, the evidence implies that garlic does not have a clinically relevant effect on total cholesterol. Garlic may have other beneficial effects for cardiovascular health. Small effects have been reported for lowering blood pressure. In addition, data from pre-clinical and epidemiological studies suggest that garlic may have effects on cancer prevention [30, 31]. It is possible that, even though each of these single effects is small, they clinically operate in concert to achieve a relevant change in mortality or morbidity. This hypothesis, however, would require testing in adequately designed trials. Large-scale, long-term studies are needed to provide useful data on any association between garlic consumption and important clinical outcomes. One attempt, reported a deceleration of atherosclerotic plaque formation after 4 years of garlic administration compared with placebo in 152 patients with atherosclerotic risk factors [32]. Although this study had an encouraging outcome, a large number of methodological limitations exist [33, 34].

Limitations of our review pertain to the potential incompleteness of the reviewed evidence. We aimed to identify all relevant RCT on the topic. The distorting effects on systematic reviews arising from publication bias and location bias are well documented [35, 36]. For this study we searched databases with a focus on the American and European literature that specialise in complementary medicine, and we included hand searches. We imposed no restrictions on language of publication, and the two reviewers independently appraised the clinical evidence. We are confident that our search strategy located all published trials on the subject.

In conclusion, the evidence based on rigorous clinical trials of garlic is not convincing. For hypercholesterolemia, the reported effects are small and may therefore not be of clinical relevance. For reducing blood pressure, few studies are available and the reported effects are too small to be clinically meaningful. For all other conditions, not enough data are available for clinical recommendations.

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