Garlic as a lipid lowering agent— a meta-analysis

ABSTRACT—Garlic supplements may have an important role to play in the treatment of hypercholesterolaemia. To determine the effect of garlic on serum lipids and lipoproteins relative to placebo and other lipid lowering agents, a systematic review, including meta-analysis, was undertaken of published and unpublished randomised controlled trials of garlic preparations of at least four weeks' duration. Studies were identified by a search of MEDLINE and the ALTERNATIVE MEDICINE electronic databases, from references listed in primary and review articles, and through direct contact with garlic manufacturers. Sixteen trials, with data from 952 subjects, were included in the analyses. Many of the trials had methodological shortcomings. The pooled mean difference in the absolute change (from baseline to final measurement in mmol/l) of total serum cholesterol, triglycerides, and high-density lipoprotein (HDL)-cholesterol was compared between subjects treated with garlic therapy against those treated with placebo or other agents. The mean difference in reduction of total cholesterol between garlic-treated subjects and those receiving placebo (or avoiding garlic in their diet) was −0.77 mmol/l (95% CI: −0.65, −0.89 mmol/l). These changes represent a 12% reduction with garlic therapy beyond the final levels achieved with placebo alone. The reduction was evident after one month of therapy and persisted for at least six months. In the dried garlic powders, in which the allicin content is standardised, there was no significant difference in the size of the reduction across the dose range of 600–900 mg daily. Dried garlic powder preparations also significantly lowered serum triglyceride by 0.31 mmol/l compared to placebo (95% CI: −0.14, −0.49). HDL-cholesterol was non-significantly lowered by 0.04 mmol/l (95% CI: −0.11, 0.03 mmol/l). Side-effects from garlic therapy, other than odour, were rare. In conclusion, use of garlic therapy, either as dried garlic preparations (in doses as low as 600 mg per day) or as fresh, high allicin yielding garlic (10–20 g per day) appears significantly to reduce total serum cholesterol over a 1–3 months period. However, more rigorously designed and analysed trials are needed.

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Introduction

Garlic (*Allium sativum*) was used as a remedy for a wide variety of ailments from as early as 1500 BC [1]. Recently most attention has been paid to the possible cardioprotective actions of garlic [2]; these include a lipid lowering action [1], antioxidant activity [3], antiplatelet action [4], favourable haemostatic effects [5] and haemodynamic properties [6].

Allicin, the principal active compound in a garlic bulb, is thought to be responsible for most of the pharmacological activity. Crushing the garlic clove activates the enzyme allinase and converts alliin to allicin. In addition to allicin, other biologically active compounds can be extracted from garlic, including alun, ajoene and various oils, mucilage and albumin [2].

The first clinical trials of garlic appeared in the literature in the late 1970s, but many suffered from significant methodological shortcomings. These included inappropriate methods of randomisation, lack of controls, poorly characterised patient groups, short duration, insufficient statistical power leading to the likelihood of a type II error, and failure to undertake an intention-to-treat analysis. Because of these problems, the authors of an overview of garlic in 1989 concluded that there was inadequate scientific justification to recommend garlic supplementation to reduce cardiovascular risk [2]. Thirteen clinical studies were identified in this earlier report, but only nine of them were randomised controlled trials. No quantitative techniques were used to estimate the size of an overall treatment effect.

Since then, a further nine randomised controlled trials have been published and commercial garlic preparations are now more widely available. Only some of the dried powder preparations contain a standardised amount of allicin [7].

Garlic supplements may have an important role to play in the treatment of hypercholesterolaemia. At least 25% of men and women aged 25–59 years have total cholesterol concentrations exceeding 6.4 mmol/l [8], which is associated with a markedly increased relative risk of premature ischaemic heart disease [9]. Since garlic products are quite acceptable to the public it is important to establish their efficacy. It was therefore decided to undertake a meta-analysis to combine the evidence that now exists. We had three *a priori* hypotheses:

- garlic acts as a lipid-lowering agent in human subjects, reducing total cholesterol and serum triglyceride whilst elevating high density lipoprotein (HDL);

- there is a dose–response relationship between the amount of garlic consumed and the degree to which blood levels are reduced; and
- the magnitude of the lipid lowering effect observed with dried garlic preparations is greater than with non-powder preparations.

Method

Identification of previous studies

A computerised literature search was conducted with DataStar on the MEDLINE database, using the terms (i) 'GARLIC' and (ii) 'LIPIDS' or 'BLOOD PRESSURE' in combination, to identify all published trials involving garlic between 1966 and July 1992. A search of the electronic ALTERNATIVE MEDICINE database, maintained by the British Library of Medicine, was also undertaken using the term 'GARLIC'. In addition, published reviews, reference lists from clinical trials, and conference abstracts were examined. To identify unpublished studies, letters were sent to manufacturers of garlic preparations and authors of published reports using the compound.

For inclusion in the meta-analysis, studies had to meet two methodological criteria. First, there had to be at least two treatment groups and, secondly, allocation to the groups must have been by formal randomisation. Studies which used historical controls were excluded. In addition, since the review was confined to the medium and long-term effects of garlic on serum lipids, trials of less than four weeks or which did not include measurement of serum lipids were also excluded.

Data extraction

Data were independently extracted from the published reports by both authors and disagreements resolved by discussion. For each trial, the following were documented:

a   country of origin;
b   study population;
c   number of subjects;
d   baseline cholesterol level;
e   type of garlic preparation (including whether or not the allicin component was standardised) and dose regimen used;
f   nature of the control group;
g   method of allocation;
h   extent of blinding;
i   parallel group versus cross-over design;
j   duration of treatment;
k   method of analysis;
l   laboratory method used to measure lipid levels;
m   withdrawals; and
n   adverse effects.

Reports which appeared only in non-English language journals were examined with the assistance of a translator.

In trials where either the methods were unclear or the results not expressed in a form which allowed extraction of the necessary key data, the individual investigators were asked by letter for the required information. Nine of the 13 investigators responded to our request, but only three could provide the data requested.

Quality assessment

The methodological quality of the studies included in the review was assessed using a simplified scheme described by Chalmers [10]. This involves assessing three dimensions of trial methodology that are important potential sources of bias:

- the quality of the random allocation (ie control of selection bias at entry);
- whether the primary analysis included every person entered into the randomised cohorts (ie control of selection bias after entry); and
- whether the assessors of outcome(s) were unaware of the group to which individuals in the trial had been assigned (ie control of bias in assessing outcome(s)).

A three-point rating scale was used for each of the three dimensions (ranging from a score of 3 if the effort to control potential bias had been maximal, through to 1 if there had been little or no such effort). In two studies where the methods used to control these sources of bias were unclear the investigator was asked for clarification [11,12].

Data analysis

The effect of garlic on serum cholesterol, serum triglyceride, and serum HDL-cholesterol was assessed independently. It was measured as the difference (in mmol/l) between the mean change in serum lipid values (baseline–final value) in the two groups. The variance of this difference should be calculated using the paired baseline and final lipid measurements for each individual, but only two trials [13,14] presented sufficient information to do this.

For the remaining trials a conservative approach was adopted: the variance of the difference between means was calculated assuming that the baseline and final lipid measurements were unpaired.

A standard error (se) of the size of the effect (x_1-x_0) was calculated for each trial independently using the following formula.

$$se(x_1-x_0) = \frac{sd_1}{n_1} + \frac{sd_0}{n_0}$$

where x_1 and x_0 are the mean changes in the treatment and control groups, respectively, sd_1 and sd_0 the standard deviations, and n_1 and n_0 the number of subjects in the same groups.

In the results section, a negative treatment effect

Table 1. Summary of randomised controlled trials not included in meta-analysis

Author Year [Ref]	Country	Participants	No. of subjects	Type of garlic	Duration (weeks)	Results	Reason for exclusion
Lutomski 1984 [17]	Poland	CHD	82	Oil	12	CHOL: ↔ TRIG: ↔	Insufficient data
Ernst 1985 [11]	Poland	HL	10	Dried (S)	4	CHOL: ↓↓ TRIG: ↓↓ HDL: ↓	Method of allocation unclear Baseline results not available
Luley 1986 [12]	Germany	HL	34	Powder	6	CHOL: ↔ TRIG: ↓ HDL: ↑	Insufficient data
Rotzch 1993 [18]	Germany	HL	24	Dried (S)	6	TRIG: ↓↓ *	Total serum cholesterol not measured

CHD = subjects with pre-existing coronary heart disease; CHOL = cholesterol; HDL = HDL-cholesterol; HL = hyperlipidaemic subjects; (S) = standardised allicin content; TRIG = triglyceride; ↓ = non-significant decrease; ↓↓ = statistically significant decrease; ↑ = increase; ↔ = unchanged.
* Changes seen in response to a fat-rich diet.

indicates a lowering of serum lipids with active intervention. Where results were reported in mg/dl, these were converted to mmol/l. For the two cross-over trials, only data from the first phase of the study were included in the analysis in order to avoid problems of carry-over effects or treatment-period interactions. In all analyses we endeavoured to use data based on all cases allocated, rather than limit to those which complied with the randomised treatment regime. This was possible in 11 of the trials.

A technique described by Bracken [15] was used to pool the effect sizes from individual studies. This is based on a fixed-effect model which assumes that the pooled effect size reflects the typical effect only of trials entered in the analysis. The pooled effect size is a weighted average of individual effects, with weights inversely proportional to the variance of each individual effect. Ninety-five per cent confidence intervals were calculated for the pooled effect size. Tests of heterogeneity were performed using the Mantel–Haenszel method [16].

Results

Description of trials identified

A total of 25 randomised controlled trials were identified which included an examination of the effect of garlic on serum lipid levels (including one trial 'in press' and one published only as a letter to the editor [11]). In five trials the follow-up was less than a month, and in three the data were insufficient to quantify the treatment effect in a form suitable for comparison with the other studies [11,12,17]. These trials were excluded when attempts to obtain this information from the investigators and the manufacturers proved unsuccessful (Table 1). The other excluded trial measured the effect of garlic therapy on HDL$_2$-cholesterol and triglycerides but not on total cholesterol [18]. The remaining 16 trials [13,14, 19–32] (which included data from 952 subjects) were all eligible for inclusion. Their methodological characteristics are summarised in Table 2.

Fourteen trials used a parallel group design, and the remaining two were cross-over studies [20,25]. Two trials were conducted in an open-label fashion [13,21], a further two were single-blind [19,23] and all the remainder were double-blind. Thirteen were placebo-controlled. One trial compared raw garlic added to a normal diet against a control group who were instructed to avoid garlic in their normal diet [21]. Agents used as the control group in the other two trials were bezafibrate [30] and a combination of a diuretic and reserpine, respectively [23]. All but one [13] of the trials were conducted in both men and women using a broad range of clinical entry criteria. None of the studies involving non-powder garlic preparations was conducted specifically in hyperlipidaemic patients. In contrast, five of the trials involving garlic powder preparations included patients on the basis of their lipid levels [25,27,28,30,32]. Only three trials required participants to have sustained elevation of serum lipids after a run-in phase [20,27,32]. In two trials this lasted only 14 days [27,32]; in the trial comparing garlic against bezafibrate [30], the run-in phase was six weeks, during which time patients were required to take placebo tablets (single-blind).

The total daily dose of garlic ranged from 600–900 mg of dried garlic powder (in the powder preparations), equivalent to 1.8–2.7 g of fresh garlic per day.

Table 2. Summary of trials included in meta-analysis

Author Year [Ref]	Country	Participants	Type of garlic	Dose per day	Control	Design	Blinding	No. of subjects	Duration	Baseline cholesterol (mmol/l)	Analysis
Non-powder garlic preparations											
Bhushan 1979 [13]	India	H	Fresh	10 g	N	PG	O	25	2M	6.19	NS
Bordia 1981 [19]	India	CHD	Oil	0.25 mg/kg	P	PG	S	68	10M	5.45	ORT
Barrie 1987 [20]	USA	H	Oil	18 mg	P	CO	D	20	4W	NS	NS
Lau 1987 [14]	USA	H	Extract	NS	P	PG	D	32	6M	7.92	ORT
Gadkari 1991 [21]	India	H	Fresh	10 g	N	PG	O	60	2M	5.53	NS
Garlic powder preparations											
Sitprija 1987 [22]	Thailand	DIA	Spray	700 mg	P	PG	D	33	1M	4.72	ORT
Kandiziora 1988 [23]	Germany	HTN	Dried (S)	600 mg	RD	PG	S	40	12W	7.21	ITT
Kandiziora 1988 [24]	Germany	HTN	Dried (S)	600 mg	P	PG	D	40	12W	7.59	ITT
Plengvidhya 1988 [25]	Thailand	HL	Spray	700 mg	P	CO	D	30	2M	7.32	NS
Auer 1990 [26]	Germany	HTN	Dried (S)	600 mg	P	PG	D	47	12W	NS	NS
Mader 1990 [27]	Germany	HL	Dried (S)	800 mg	P	PG	D	261	4M	6.84	ORT
Vorberg 1990 [28]	Germany	HL	Dried (S)	900 mg	P	PG	D	40	16W	NS	NS
Kiesewetter 1991 [29]	Germany	SA	Dried (S)	800 mg	P	PG	D	60	4W	NS	NS
Holzgartner 1992 [30]	Germany	HL	Dried (S)	900 mg	B	PG	D	94	12W	7.39	ITT
Santos 1993 [31]	UK	NS	Dried (S)	900 mg	P	PG	D	60	6M	6.98	ORT
Jain 1993 [32]	USA	HL	Dried (S)	900 mg	P	PG	D	42	12M	7.00	NS

B = bezafibrate; CHD = subjects with pre-existing coronary heart disease; CO = cross-over study; D = double blind; DIA = diabetic subjects; H = healthy subjects; HL = hyperlipidaemic subjects; HTN = hypertensive subjects; ITT = intention-to-treat analysis; M = months; N = no garlic control; NS = not stated; O = open label; ORT = on randomised treatment; P = placebo; PG = parallel group study; RD = reserpine/diuretic combination; S = single blind; (S) = standardised allicin content; SA = subjects with increased spontaneous aggregation; W = weeks.

In the non-powder preparations the daily dose ranged from 10 g of raw garlic to 18 mg of garlic oil. The median duration of therapy was 12 weeks (range four weeks to 10 months).

The quality assessment of the trials was generally poor (Fig 1), with the notable exception of the trial comparing garlic powder and bezafibrate which scored the maximum number of points for each criterion [30]. Only one other trial report provided any information on the techniques used to achieve effective randomisation [27], and only three formally stated that an intention-to-treat analysis had been used [23,24,30]. In six reports the analysis was confined to those patients receiving randomised therapy at the conclusion of the treatment period. In the remainder it was not possible to confirm from the report which type of analysis had been used. It is difficult to disguise garlic capsules or tablets because of their odour. Although several studies attempted to do so, it is unclear from the data whether this was effective. None of the trials referred to any attempts to assess compliance with therapy. Although the lack of blinding to the medication on trial may produce problems in comparing rates of adverse effects, it is less likely to affect interpretation of the serum lipid levels based on laboratory measurements. In each case, a standardised procedure was used which had been appropriately referenced.

Effects on total cholesterol

The mean difference in reduction of total cholesterol between garlic-treated subjects and those receiving placebo (or avoiding garlic in their diet) was −0.77 mmol/l (95% CI: −0.65, −0.89 mmol/l). This effect was significantly greater among subjects receiving non-powder garlic preparations (−0.99 mmol/l; 95% CI: −0.83, −1.16 mmol/l) than those receiving garlic powder preparations (−0.51 mmol/l; 95% CI: −0.33, −0.69 mmol/l) (Fig 2); however, the non-powder preparations showed significant heterogeneity (chi-square: 21.87; 4 df $p = 0.00021$). All further analyses were therefore confined to the powder preparations only.

The effect of increasing dosages of garlic amongst these powder preparations did not produce any clinically or statistically significant difference in the effect across the dose range of 600–900 mg of dried garlic powder per day.

The effect of garlic therapy on serum cholesterol progressively increased between months one and three
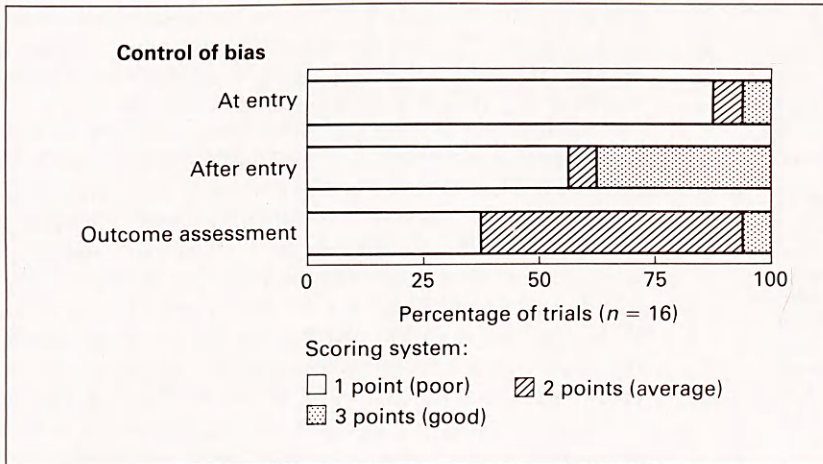
Fig 1. *Overall methodological quality of trials included in the meta-analysis (n = 16) based on an assessment of control of selection bias at entry and after entry, and control of assessment bias.* Percentage of trials scoring 3 points (full credit), 2 points (some credit), and 1 point (no credit). Results for individual studies are shown in Table 1.

(Fig 3). The reduction in serum cholesterol at six months was less than that seen at three months, but these data came from a single trial [31] and the confidence intervals were wide.

Effect on triglycerides and high density lipoprotein cholesterol

Eight trials (all garlic powder preparations) contributed data to the comparison of the effects of garlic against placebo on serum triglyceride levels [24–28, 31,32]. Garlic therapy reduces the serum triglyceride level by 0.31 mmol/l compared with placebo (95% CI: –0.14, –0.49), a reduction of 13%. Treatment with garlic powder results [23,25,31,32] in a small, insignificant reduction in HDL-cholesterol levels (–0.04 mmol/l, 95% CI: –0.11, 0.03 mmol/l). Only one trial has been reported so far which compares the effect of garlic therapy against a known lipid lowering agent, bezafibrate. Although both agents were effective, they did not differ significantly.

Adverse effects

Seven of the trials mentioned that adverse effects were not significantly increased as a result of garlic therapy, but only three documented these in detail. Among the studies using the dried garlic powder preparation, which is reported to be odour-controlled, only four kept records documenting the incidence of this effect [26,27,31,32]. In the largest of these trials [27], after 16 weeks therapy, 16% of subjects taking the active preparation complained of a garlic smell compared with 5% on placebo. When the results from the other trials were also included, the overall likelihood of experiencing odour when using a garlic preparation was nearly four times that with placebo (3.76, 95% CI: 1.82, 7.80). None of the studies reported any significant increase in other side-effects arising from garlic therapy.

Discussion

Garlic, in powder or non-powder form, can significantly lower serum lipid levels over a 1–3 months period. Serum cholesterol falls 8% with dried powder preparations and 15% with non-powder preparations, although the latter reduction must be interpreted with

Fig 2. *Effect size (in mmol/l) of garlic therapy versus placebo (or avoidance of garlic) on total serum cholesterol for individual trials and overall for non-powder preparations, garlic powder preparations, and any preparation.* Bars indicate 95% confidence interval. Tests for heterogeneity among sizes of treatment effects: (i) in non-powder preparations, chi-square 21.87; 4 df, $p = 0.00021$; (ii) garlic powder preparations, chi-square 15.36; 8 df, NS.
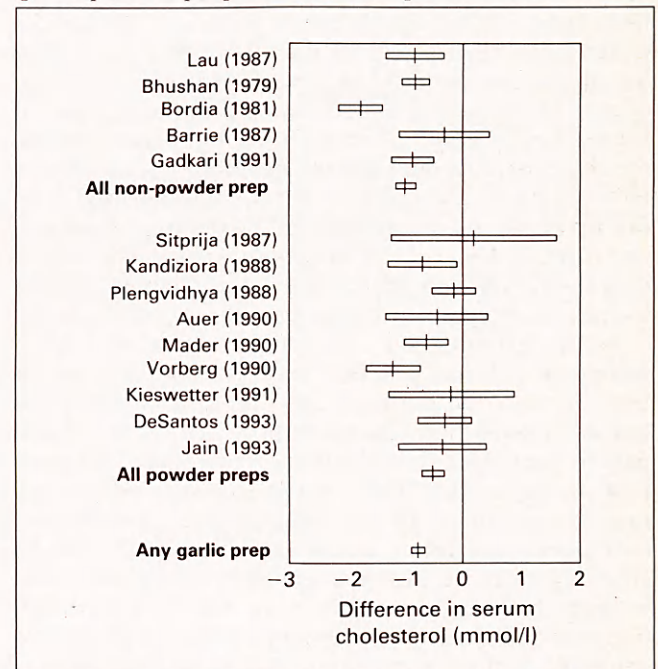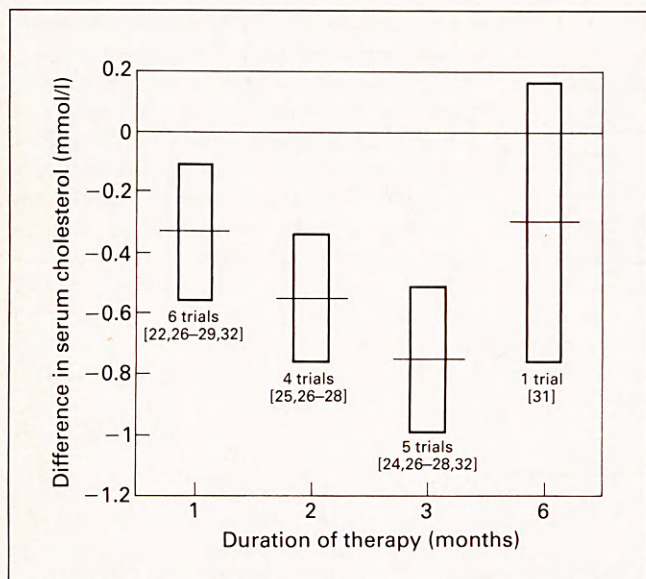
Fig 3. *Summary effect size (in mmol/l) of garlic powders versus placebo on total serum cholesterol with 1, 2, 3 and 6 months' duration of therapy.* Bars indicate 95% confidence interval. References to trials included are in square brackets.

caution, given the heterogeneity associated with the currently available trials. Serum triglyceride levels also drop significantly, whilst HDL-cholesterol is essentially unchanged. There is insufficient information to comment on the use of non-powder preparations in reducing other lipid parameters.

Amongst the garlic powder preparations these effects appear to be similar across the daily dose range of 600–900 mg. It is not possible to give an exact equivalent dose of fresh garlic, since there is considerable variation in clove size and allicin content depending on where the product is grown. However, 600 mg approximately equates to one medium size clove of fresh Chinese garlic per day (P Josling; personal communication). Adverse effects, including odour, appear to be relatively uncommon with the standardised powder preparations, particularly in lower doses. However, the threefold increased likelihood of a garlic odour with the 'odour-controlled' dried garlic tablets may be socially unacceptable to some people.

Before generalising from the results of this meta-analysis to clinical practice, several important limitations need to be highlighted. The meta-analysis was based on published reports rather than on individual patient data (with the exception of two trials). A recent report suggests that such an approach may be misleading, because of problems associated with publication bias, patient exclusion, and length of patient follow-up [33]. Although we tried to meet these concerns in part by approaching investigators to obtain additional unpublished data to clarify areas of uncertainty, the generally enthusiastic response of these investigators

was not matched with making the necessary data available. It is possible that there are also some unpublished trials that may show less favourable results which have not been identified despite systematic efforts.

The studies involving garlic which were identified have been largely restricted to Thailand, Germany and the USA. The total patient experience in randomised trials (1,365 individuals) is still quite small. Although uncontrolled studies suggest that dried garlic powder preparations are generally well tolerated with a low incidence of adverse effects, this needs to be confirmed in larger randomised trials. In any future trials the failure generally to incorporate an adequate run-in phase, which includes the use of dietary therapy, needs to be addressed, as also does the failure to assess the subjects' compliance with the treatment protocol.

Unfortunately, five of the trials were not analysed on an intention-to-treat basis because of lack of available data. The treatment effect may have been overestimated in these studies. On the other hand, the calculation of the standard deviation for the change in serum lipid values (baseline to final value) in both the active treatment and the control groups assumed a non-paired analysis in most cases, which would tend to overestimate the true standard deviation and therefore widen the confidence interval around the treatment effect.

The direction of the findings is supported by the other randomised controlled trials of shorter duration and those with insufficient data to be included in the formal pooling of the overall treatment effect (see Table 1). Failure to include these studies, particularly those with insufficient data, is therefore unlikely to have materially affected these results.

The similar effect on lipid levels of dried garlic powder and of bezafibrate is promising. Data from systematic reviews of the magnitude of lipid lowering with other non-pharmacological measures, such as oat products [34] and dietary advice [34], suggest much more modest reductions in total serum cholesterol. A step 1 lipid lowering diet reduced cholesterol by only 0–4% over a period of six months to six years [35]. Only when diets more intensive than step 2 were used was serum cholesterol reduced by 13–15% in various population sub-groups. Further trials are now required comparing dried powder garlic preparations with existing hypolipidaemic drugs after a period of appropriate dietary intervention.

Garlic is not a licensed medication and there is not enough evidence to recommend garlic therapy as an effective lipid lowering agent for routine clinical use. However, there is also no evidence to suggest it is harmful. The currently available data support the likelihood of garlic therapy being beneficial, at least over a few months. Resolving this situation will require further trials that avoid the methodological problems of earlier studies and, in particular, last long enough and have adequate statistical power to detect whether any clear-cut benefits arise from the use of garlic.

References

1 Mansell P, Reckless JPD. Garlic (editorial). *Br Med J* 1991;**303**:379–80.

2 Kleijnen J, Knipschild P, Ter Riet G. Garlic, onions and cardiovascular risk factors. A review of the evidence from human experiments with emphasis on commercially available preparations. *Br J Clin Pharmacol* 1989;**28**:535–44.

3 Phelps S, Harris WS. Garlic supplementation reduces the susceptibility to oxidation of apolipoprotein B-containing lipoproteins. *Lipid* 1993;**28**:475–7.

4 Kiesewetter H, Jung F, Mrowietz C, Pindur G, *et al.* Effects of garlic on blood fluidity and fibrinolytic activity: a randomised placebo controlled double blind study. *Br J Clin Pract* 1990;**S69**:24–9.

5 Chutani SK, Bordia AK. The effect of dried versus raw garlaic on fibrinolytic activity in man. *Atherosclerosis* 1981;**38**:417–21.

6 Brosche T, Platt D, Dorner H. The effect of a garlic preparation on the composition of plasma lipoproteins and erythrocyte membranes in geriatric subjects. *Br J Clin Pract* 1990;**S69**:12–9.

7 Pentz R, Guo Z, Muller B, Aye RD, Siegers CP. Standardisierung von Knoblauchpraparaten. *Deutsche Apotheker Zeitung* 1992;**132**:1779–82.

8 Mann JI, Lewis B, Shepherd J, Winder AF, *et al.* Blood lipid concentrations and other cardiovascular risk factors: distribution, prevalence, and detection in Britain. *Br Med J* 1988;**296**:1702–6.

9 Martin JM, Hully SB, Browner WS, Kuller LH, Wentworth D. Serum cholesterol, blood pressure, and mortality: implications from a cohort of 361,662 men. *Lancet* 1986;**ii**:933–6.

10 Chalmers I, Enkin M, Keirse MJNC, eds. *Effective care in pregnancy and childbirth.* Oxford: Oxford University Press, 1985.

11 Ernst E, Weihmayr T, Matrai A. Garlic and blood lipids. *Br Med J* 1985;**291**:139.

12 Luley C, Lehmann-Leo W, Moller B, Martin T, Schwartzkopff W. Lack of efficacy of dried garlic powder in patients with hyperlipoproteinaemia. *Arnzeim Forsch* 1986;**36**:766–8.

13 Bhushan S, Sharma SP, Singh SP, Agrawal S, *et al.* Effect of garlic on normal blood cholesterol level. *Ind J Physiol Pharmacol* 1979;**23**: 211–4.

14 Lau BHS, Lam F, Wang-Cheng R. Effect of an odor-modified garlic preparation on blood lipids. *Nutrition Res* 1987;**7**:139–49.

15 Bracken MB. Statistical methods for analysis of effects of treatment in overviews of randomized trials. In: Sinclair JC, Bracken MB, eds. *Effective care of the newborn infant.* Oxford: Oxford University Press, 1992:13–8.

16 Cochran WG. The combination of estimates from different experiments. *Biometrics.* 1954;**10**:101–29.

17 Lutomski J. Klinische Untersuchungen zur therapeutischen Wirksamkeit von Ilja Rogoff Knoblauchpillen mit Rutin. *Z Phytother* 1984;**5**:938–42.

18 Rotzsch W, Richter V, Rassoul F, Walper A. Postprandiale Lipamie unter Medikation von Allium sativum. *Arzneim Forsch* 1992;**42**:1223–7.

19 Bordia AK. Effect of garlic on blood lipids in patients with coronary heart disease. *Am J Clin Nutr* 1981;**34**:2100–3.

20 Barrie SA, Wright JV, Pizzorno JE. Effects of garlic oil on platelet aggregation serum lipids and blood pressure in humans. *J Orthomolec Med* 1987;**2**:15–21.

21 Gadkari JV, Joshi VD. Effect of ingestion of raw garlic on serum cholesterol level, clotting time and fibrinolytic activity in normal subjects. *J Postgrad Med* 1991;**37**:128–31.

22 Sitprija S, Plengvidhya C, Kangkaya V, Bhuvapanich S, Tunkh Yoon M. Garlic and diabetes mellitus phase II clinical trial. *J Med Assoc Thai* 1987;**70**:223–7.

23 Kandziora J. The blood pressure lowering and lipid lowering effect of a garlic preparation in combination with a diuretic. *Arzt Forschung* 1988;**3**:1–8.

24 Kandziora J. Antihypertensive effectiveness and tolerance of a garlic medication. *Arzt Forschung* 1988;**1**:1–8.

25 Plengvidhya C, Chinayon S, Sitprija S, Pasatrat S, Tunkh Yoon M. Effects of spray dried garlic preparation on primary hyperlipoproteinaemia. *J Med Assoc Thai* 1988;**71**:248–52.

26 Auer W, Eiber A, Hertkorn E, Hoehfeld E *et al.* Hypertension and hyperlipidemia: garlic helps in mild cases. *Br J Clin Pract* 1990;**S69**:3–6.

27 Mader FH. Treatment of hyperlipidemia with coated garlic tablets. Double-blind study with 261 patients in 30 general practices. *Der Allgemeinarzt* 1990;**8**:435–40.

28 Vorberg G, Schneider B. Therapy with garlic: results of a placebo-controlled double-blind study. *Br J Clin Pract* 1990;**S69**:7–11.

29 Kiesewetter H, Jung F, Pindur G, Jung EM, *et al.* Effect of garlic on thrombocyte aggregation, microcirculation, and other risk factors. *Int J Clin Pharmacol Ther Toxicol* 1991;**29**:151–5.

30 Holzgartner H, Schmidt U, Kuhn U. Comparison of the efficacy and tolerance of a garlic preparation versus bezafibrate. *Arzneim Forsch* 1992;**42**:1473–7.

31 De Santos OS, Grunwald J. Effect of garlic powder tablets on blood lipid and blood pressure. A six month placebo-controlled double-blind study. *Br J Clin Res* 1993;**4**:37–44.

32 Jain AK, Vargas R, Gotzkowsky S, McMahon FG. Can garlic reduce serum lipids?—a controlled clinical study. *Am J Med* 1993;**94**:632–5.

33 Stewart LA, Parma MKB. Meta-analysis of the literature or of individual patient data: is there a difference? *Lancet* 1993;**341**:418–22.

34 Ripskin CM, Keenan JM, Jacobs DR, Elmer PJ, *et al.* Oat products and lipid lowering. A meta-analysis. *JAMA* 1992;**267**:3317–25.

35 Ramsay LE. Dietary reduction of serum cholesterol concentration: time to think again. *Br Med J* 1991;**303**:953–7.

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