



Garlic *Allium sativum*

Both food and medicine, garlic is a largely universal staple herb popular throughout history. Pharmacist and naturopath Lesley Braun investigates its role for today's healthcare professional.

Universally used as a food and flavouring agent, garlic has also been used as a therapeutic remedy since ancient times. Folklore has it that garlic was used in ancient Egypt to increase workers' resistance to infection and later as a topical treatment for wound infection. However, it wasn't until several millennia later that the antimicrobial activity of garlic was confirmed finally in the laboratory, reportedly by Louis Pasteur. Before the advent of antibiotics, garlic was widely used to prevent and treat infection, such as in World War Two. Since then, its use as a 'natural antibiotic' has declined and its role in preventing and treating age-related diseases has been extensively explored.

Garlic belongs to the genus *Allium*, which comprises of over 600 known species such as *Allium cepa* (onion) and *Allium porrum* (leek). The garlic bulb, and oil extracted from it, is used medicinally. Garlic bulbs contain a complex mixture of phytochemicals that are likely to interact synergistically to produce the effects seen clinically. Of these, the organosulphur compounds have received the most attention and are considered the most important for therapeutic activity and the herb's pungent odour.

Alliin is one of the most abundant organosulphur constituents in garlic and considered the parent substance for several key pharmacologically active degradation products. When garlic is chewed, crushed, bruised or cut, the enzyme alliinase converts alliin into thiosulphinat allicin. According to Commission E, 1 mg of alliin produces 0.458 mg of allicin.

Cardiovascular effects

Garlic exerts numerous important pharmacological activities. It has both direct and indirect anti-oxidant activity, enhancing endogenous anti-oxidant systems such as glutathione, super-

oxide dismutase (SOD), catalase and glutathione peroxidase.⁴⁵ Both antiplatelet and antithrombotic properties have been observed in several human studies, however the method of garlic preparation appears to influence the degree of activity.¹⁻³ According to *in-vitro* research, garlic inhibits cholesterol biosynthesis by deactivating HMG-CoA reductase without changing the amount of enzyme present, thereby accounting for its modest cholesterol-lowering effects.⁴ Animal studies suggest that garlic affects both the renin-angiotensin and nitric oxide systems, resulting in a clinically significant hypotensive effect.⁵ Fresh garlic extracts and garlic oil have been shown to inhibit cyclooxygenase activity in test-tube and animal studies.^{6,7} Additionally, evidence from *in-vitro*, animal and human research has demonstrated that garlic supplementation significantly reduces the atherosclerotic process.⁸⁻¹³

Due to its many actions on known cardiovascular disease risk factors and on the cardiovascular system in general, it is not surprising that there is considerable epidemiological and clinical evidence that regular garlic supplementation reduces cardiovascular risk.¹⁴ Intervention studies using high-dose supplements have also produced interesting results.

A meta-analysis of seven clinical trials using a commercial garlic preparation (Kwai, Lichtwer Pharma, UK) found that, in three trials, garlic produced a significant reduction in systolic blood pressure and, in four trials, diastolic BP also reduced.¹⁵ Since then, a slow-release garlic product (Allicor, Agrochemie Zlín sro, Czech Republic) was tested in a double-blind, randomised clinical trial involving 85 patients with mild-to-moderate hypertension. This active treatment reduced both systolic and diastolic BP as compared to placebo.¹⁶ The doses varied between 600-900 mg daily in divided doses (delivering approximately 5-6 mg of allicin potential).



Factfile

Indications	infections, wounds, respiratory conditions, diarrhoea, rheumatism, heart disease, diabetes
Pharmacology	anti-oxidant, diaphoretic, expectorant, antispasmodic, antiseptic, bacteriostatic, antiviral, hypotensive, anthelmintic, antiplatelet, antithrombotic
Constituents	organosulphur compounds (e.g. alliin); protein; enzymes (e.g. alliinase, catalase); amino acids (e.g. arginine, lysine, threonine and tryptophan); lipids; phytic acid; saponins; β -sitosterol; polyphenols; moderate levels of selenium, germanium, vitamins A and C and small quantities of vitamin E, zinc, betacarotene, chromium and iron
Products	capsules, extract, oil, powdered bulb, syrup, tablets, tea
Therapeutic dosage	bulb: 2–4 g tid dried, 4 g/day fresh tincture: 2–4 mL (1:5 in 45% alcohol) tid oil: 0.03–0.12 mL tid juice: 2–4 mL syrup: 2–8 mL
Precautions	contraindicated in pregnancy or lactation; in surgery patients and those with peptic ulcers, hypothyroidism, allergies to Liliaceae family. Children should have doses diluted if at all, as fatalities have been recorded. Some people experience GI complaints and dizziness on high-dose fresh garlic
Interactions	can potentiate anticoagulants and theoretically enhance hypoglycaemic effects of antidiabetic drugs

Effects on blood lipids are less consistent. In 2000, a meta-analysis of 13 clinical trials concluded that garlic reduces total cholesterol levels significantly more than placebo, however, the effects can only be described as modest.¹⁷

According to one randomised, double-blind, placebo-controlled trial, long-term use of garlic powder supplements significantly reduces the expected increase in arteriosclerotic plaque volume by 5–18 per cent, with a slight regression also possible. The study involved 152 volunteers and focused on plaque volumes in carotid and/or femoral arteries.¹²

Cancer protection

Many studies have reported antineoplastic effects for both the oil- and water-soluble allyl sulphur compounds from garlic.¹⁸ Diallyl disulphide, one of the most studied oil-soluble organosulphur compounds, inhibits the proliferation of human tumour-cell lines for colon, lung and skin cancer and has demonstrated antineoplastic activity against both hormone-dependent and hormone-independent breast-cancer cell lines.^{19,20} Additionally, ajoene induces apoptosis in human leukaemic cells according to *in-vitro* tests²¹, whereas alliin inhibits proliferation of human mammary, endometrial, and colon-cancer cells.²²

A 2001 critical review of the epidemiological evidence suggests a preventive effect for dietary garlic consumption in stomach and colorectal cancers, but not other cancers.²³ More specifically, case-control studies suggest that raw and/or cooked garlic eaten at least once a week confers protection against

gastric cancer, whereas twice-a-week consumption is required for protection against colorectal cancer.

Infection control

As originally observed in ancient times, garlic has substantial antimicrobial activity. It exerts both direct and indirect effects against various pathogens, as it enhances macrophage and T-lymphocyte function²⁴ and has direct antibacterial, antifungal, antiviral and antiparasitic activity. Both ajoene and alliin are chiefly responsible for these effects. Of interest, several *in-vitro* and *in-vivo* tests have shown that garlic has activity against *H. pylori*^{25–27}, with two studies demonstrating that a combination of garlic and omeprazole produces synergistic effects.^{28,29}

In practice, garlic bulbs, home-brewed garlic concoctions and commercially prepared garlic products are used for myriad indications. Home brews often contain a mixture of garlic, honey, possibly lemon juice, ginger and a variety of other kitchen ingredients and are mainly used to ward off an impending cold or flu. Although clinical studies are unavailable, this remedy has a wide following and is anecdotally considered to be very effective.

Commercially produced garlic supplements are also popular for common URTIs and are sometimes combined with horseradish to provide symptomatic relief. A 12-week double-blind, randomised study involving 146 people demonstrated that alliin-containing garlic preparations significantly reduce the incidence of colds and accelerate recovery compared to placebo.³⁰ More specifically, the number of symptom days in the placebo group was 5.01 compared to 1.52 days in the



garlic-treated group. Additionally, garlic reduced the incidence of developing a second cold whereas placebo did not.

Ajoene-containing creams have been investigated for effects against *tinea pedis*, *tinea corporis* and *tinea cruris* in one study. The trial compared three different strengths of ajoene cream (0.4%, 0.6% and 1%) to 1% terbinafine (e.g. Lamisil, Novartis) applied twice daily, and found the cure rate was 72% for 0.6% ajoene, 100% for 1% ajoene, and 94% for 1% terbinafine after 60 days.³¹

Although several *in-vitro* and *in-vivo* tests have shown garlic to be effective against *H. pylori*, the few small clinical trials conducted to date have produced inconsistent results.³²⁻³⁴ One small pilot study of dyspeptic patients with confirmed *H. pylori* infection found that treatment with 4 mg garlic oil capsules taken four times daily for 14 days did not alter symptoms or lead to *H. pylori* eradication.³⁴ Alternately, another small study using a much larger dose of garlic oil (275 mg) tid (800 mcg allicin per capsule), either as stand-alone treatment or in combination with omeprazole (20 mg twice a day) found both treatments produced similar results.³⁵ These results were confirmed in another small clinical study.³⁶

Answers for some inconsistent results

A difficulty in interpreting the clinical data for garlic is that different researchers use different preparations and many do not appear to have been tested for the presence of important constituents, such as alliin. Additionally, while fresh and powdered garlic contain both alliin and the enzyme alliinase responsible for its transformation, it is not known whether all other forms contain both substances and have sufficient alliin-releasing potential. As such, it would not be surprising to find that the standard of garlic preparations used in intervention studies is likely to vary considerably and have a marked influence on results. The following example clearly illustrates the point. According to a 2001 experiment, substantial differences were found between Kwai garlic tablets manufactured before 1993 and those manufactured after this date. Comparison of the two forms found that pre-1993 tablets disintegrated more slowly, protecting alliinase from acid exposure and inactivation whereas the later tablets released only one-third as much allicin.³⁷ This is noteworthy because the pre-1993 Kwai tablets produced a majority of the positive results obtained in various chole-

sterol intervention studies whereas post-1993 Kwai tablets generally produced poor results.

Besides the influence of variable product quality, treatment time frames and treatment doses also differ considerably. For instance, doses between 600–9000 mg daily of various garlic preparations have been investigated in hyperlipidaemia.

Safety and adverse effects

Oral intake of garlic is considered safe but is sometimes associated with mild and transient adverse effects, such as bad breath and body odour, nausea, heartburn, flatulence, abdominal discomfort and diarrhoea.³⁹ One study using a dose of 900 mg garlic powder (standardised to 1.3% alliin) reported headache, myalgia and fatigue as adverse effects.⁴⁰ Allergic reactions have also been reported.

Topical preparations can cause a transient burning sensation and contact dermatitis can also occur.^{41,42}

Avoid high doses of garlic (>4 g daily) in patients taking anticoagulants, unless under professional supervision, as there is an increased risk of bruising and bleeding. Theoretically, garlic supplements may produce additive cholesterol-lowering and antihypertensive effects when combined with pharmaceutical antihypertensive and lipid-lowering drugs. The effects may be beneficial under supervision. Additionally, high-dose garlic-oil supplements appear to enhance the effects of omeprazole in *H. pylori* eradication, suggesting a beneficial interaction.⁴⁵

It is still unclear whether garlic affects cytochrome P (CYP) enzymes, as results from *in-vitro*, animal and human studies are confusing. Recently, an interaction between saquinivir and garlic has been reported, suggestive of a CYP induction effect, but human tests do not support this theory.⁴² Until further investigation is undertaken, avoid concurrent use of garlic in people taking saquinivir.

As a general safety precaution, people with bleeding abnormalities should avoid high dietary and supplemental intakes of garlic and use should be suspended one week prior to major surgery. If garlic or ajoene is being used as part of a topical application, a test patch is advised before more widespread application.

Garlic has an encouraging future as research accumulates to show it has many different beneficial effects. However, to



clarify the role of garlic supplements in practice, further clinical studies are required that use standardised garlic formulations with known levels of key ingredients and allicin-releasing ability. ▸

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CPE article 13: garlic



Pharmacists This unit is worth half-an-hour CPE credit. ACPP members and CPE self-assessment program subscribers can read the Garlic monograph, then circle the appropriate answers and complete the form below the questions, using a black pen. Photocopy the page and **fax** it to the **Australian College of Pharmacy Practice on 02 6273 8988**, or **post** to: **ACPP, PO Box 7007, CANBERRA BC ACT 2610**. Or, complete the unit **online: www.acpp.edu.au**.

Be prompt – ACPP must receive your answers by 6 September. Answers will be printed in the next *JCM* [Vol 3(5)] in Sep/Oct.

Q Circle the most appropriate answer to the following questions. More than one answer may be correct.

1 The most important constituents in garlic bulbs are considered to be

- a) vitamins
- b) minerals
- c) amino acids
- d) organosulphur compounds

2 The constituent alliin is

- a) converted into several important degradation products by the enzyme catalase
- b) converted into several important degradation products by the enzyme aliinase
- c) not necessary for garlic's pharmacological activity
- d) an amino acid

3 Garlic exerts many different effects that can influence CVD risk, such as

- a) hypotensive activity
- b) lipid-lowering activity
- c) anti-oxidant activity
- d) antiplatelet activity

4 Garlic may reduce the incidence of some cancers.

To date, epidemiological evidence suggests a protective effect against

- a) skin cancer
- b) breast cancer
- c) colorectal cancer
- d) stomach cancer

5 Although garlic is considered safe, it should be avoided or used with caution by

- a) people taking anticoagulants
- b) people with bleeding disorders
- c) people about to undergo major surgery
- d) vampires, according to folklore

CPE ARTICLE 12 ANSWERS: feverfew

JCM 2004;3(3):71 – MAY/JUNE 2004

1. b, c 2. a, c 3. b, c, d 4. a, d 5. a

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