The Longwood Herbal Task Force
(http://www.mcp.edu/herbal/default.htm) and
The Center for Holistic Pediatric Education and Research
(http://www.childrenshospital.org/holistic/)

Garlic (*Allium sativum*)

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Principal Proposed Uses: Cardiovascular: antilipemic, anti-hypertensive; antimicrobial
Other Proposed Uses: Cancer prevention

Overview

Garlic's current principal medicinal uses are to prevent and treat cardiovascular disease by lowering blood pressure and cholesterol, as an antimicrobial, and as a preventive agent for cancer. The active constituents are several complex sulfur-containing compounds that are rapidly absorbed, transformed and metabolized. Pooled data from numerous randomized trials suggest that garlic lowers total cholesterol concentrations by approximately 10% and favorably alters HDL/LDL ratios. Randomized trials also support garlic's effectiveness as a mild antihypertensive which lowers blood pressure by 5-7%. Garlic also inhibits platelet aggregation and enhances fibrinolytic activity, reducing clots on damaged endothelium. *In vitro* data suggest antiviral and antibacterial effects, but these have not been evaluated in controlled trials in humans. Epidemiologic data, *in vitro* studies and animal data suggest that garlic may help prevent some solid tumors, but no randomized trials have evaluated its effectiveness as a therapeutic agent in oncology. There are no studies evaluating its effectiveness or safety in treating children or pregnant or nursing women. Garlic is safe when eaten as food, though in some sensitive persons, it can cause gastrointestinal irritation, and of course, halitosis. Prolonged topical use has been associated with moderate burns.

Historical and Popular Uses

Need to ward off vampires? The common cold? Heart disease? Cancer? Garlic has been used for thousands of years for culinary, medicinal and spiritual purposes. Garlic has been grown

around the world, from Mediterranean climates to Siberia. Ancient Egyptians used it as a form of currency; its medical and magical powers were described on the walls of ancient temples and on papyrus dating to 1500 BC. Garlic cloves were buried in King Tut's tomb[1]. Garlic was used by the Greek physicians, Hippocrates and Galen, and during the Middle ages by Hildegard von Bingen. In the Middle Ages, garlic was used to ward off the evil eye, witches and vampires; it was also used as an aphrodisiac. In China, garlic was forbidden food for Buddhist monks because of its reputation as a sexual stimulant.

The name "allium sativum" is derived from the Celtic word "all", meaning burning or stinging, and the Latin "sativum" meaning planted or cultivated[2]. The English word, garlic, is derived from the Anglo-Saxon "gar-leac" or spear plant, referring to its flowering stalk.

Garlic has historically been used to treat earaches, leprosy, deafness, severe diarrhea, constipation and parasitic infections, and to lower fever, fight infections and relieve stomach aches.

In Traditional Chinese Medicine, garlic is known as *da suan*. It is considered a warm, bitter herb with particular effects on the Large Intestine, Spleen and Stomach meridians. It is used to lower blood pressure, to treat parasitic infections, food poisoning and tumors, and as a mild anticoagulant. It is traditionally contraindicated in patients with a yin deficiency[3-5]. Arabian herbalists use garlic to treat abdominal pain, infantile colic, diarrhea, diabetes, eye infections, snake bites, dandruff and tuberculosis[6]. African herbalists use garlic to treat respiratory infections and helminthic infections; many African families use garlic oil drops to treat childhood ear infections[7]. In Ayurvedic medicine, garlic is used to treat respiratory problems, ulcers, colic and flatulence, and garlic oil drops are used to treat earaches[8]. Several folk traditions recommend garlic as an emmenagogue or to induce abortions[9].

In the 1800's, American physicians recommended garlic inhalation as a treatment for tuberculosis. Louis Pasteur demonstrated garlic's antiseptic activity in 1858, and Albert Schweitzer used it to treat dysentery in Africa[10, 11]. During World War I, garlic poultices were used topically to prevent wound infections in much the same way as described thousands of years earlier in the Talmud. By World War II, garlic had a reputation as "Russian penicillin" so prevalent was its use in a world in which antibiotics were in short supply.

American physicians relied on garlic as an antihypertensive agent up until the late 1950's. Although it was largely abandoned by mainstream physicians as more potent cardiovascular drugs and antibiotics became available, herbalists have continued to recommend it frequently.

Garlic is thought to have diaphoretic, expectorant, antispasmodic, antiseptic, bacteriostatic, antiviral, antihelminthic and hypotensive effects; it is commonly used to treat chronic bronchitis, recurrent upper respiratory tract infections and influenza[12]. In Europe and India, garlic remedies are used to treat coughs, colds, hay fever and asthma. Many modern herbalists and folk healers still rely on garlic oil ear drops to heal the pain of a child's ear infection.

Garlic has been on the top ten lists of herbal sales for several years. Naturopathic physicians and herbalists sometimes recommend it as a topical treatment for yeast and fungal infections. The German Commission E recommends garlic as a supportive dietary measure to lower elevated blood lipids and as a preventive measure for age-dependent vascular changes; it does not note any contraindications[13]. The European Scientific Cooperative on Phytotherapy recommends garlic to prevent atherosclerosis, treat elevated blood lipids, improve circulation in patients with peripheral arterial vascular disease, and treat upper respiratory tract infections[14,15].

Botany

Medicinal species: Allium sativum

Common names: Ail, ajo, alii sativi bulbs, garlic, Russian penicillin, stinky rose, Knoblauch (Ger), Knoblauchzweibel (Ger), da suan (Chin), taisan (Jap), inniku (Jap), taesan (Kor), tafanuwa (Hausa), ayo-ishi (Igbo), kitunguusumu (Swahili), ayu (Yoruba), rasonam (Sanskrit), lasan (Hindi), lobha (Nepalese)

Botanical family: Liliaceae/Alliaceae/Amaryllidaceae

Plant description: Garlic is a bulbous perennial herb, closely related to the onion. It has a tall, erect flowering stem that reaches 2-3 feet in height. The plant has pink or purple flowers that bloom in mid to late summer. The part used medicinally is the bulb.

Where it's grown: Thought to have originated in central Asia, garlic has been cultivated in the Middle East for over 5000 years, making it one of mankind's first cultivated plants. It is now grown around the world. Plants are propagated by separating and planting individual

bulbs. The cloves are harvested in the fall as the flowers are replaced by a cluster of black seeds and the stalks begin to wither and die. Gilroy, California (just south of San Jose) claims to be the garlic capital of the world. California produces more garlic than any other state in the US. Garlic powder is prepared from the cleaned, dried, separated cloves. European standards specify that garlic supplements contain not less than 0.45% allicin[14].

Biochemistry

Garlic: Potentially Active Chemical Constituents

- Sulfur compounds: aliin, allicin, ajoene, allylpropyl disulfide, diallyl trisulfide, s-allylcysteine, vinyldithiines, S-allylmercaptocystein, and others
- Enzymes: allinase, peroxidases, myrosinase, and others
- Amino acids and their glycosides: arginine and others
- Selenium, germanium, tellurium and other trace minerals

Garlic contains at least 33 sulfur compounds, several enzymes, 17 amino acids, and minerals such as selenium[12]. It contains a higher concentration of sulfur compounds than any other *Allium* species. The sulfur compounds are responsible both for garlic's pungent odor and many of its medicinal effects. Dried, powdered garlic contains approximately 1% *alliin* (S-allyl cysteine sulfoxide)[14]. One of the most biologically active compounds, *allicin* (diallyl thiosulfinate or diallyl disulfide) does not exist in garlic until it is crushed or cut; injury to the garlic bulb activates the enzyme allinase, which metabolizes alliin to allicin[16]. Allicin is further metabolized to vinyldithiines. This breakdown occurs within hours at room temperature and within minutes during cooking[17]. Allicin, which was first chemically isolated in the 1940's, has antimicrobial effects against many viruses, bacteria, fungi and parasites[1]. Garlic oil, aged garlic and steam-distilled garlic do not contain significant amounts of aliin or allicin, but instead contain various products of allicin transformation; none appears to have as much physiologic activity as fresh garlic or garlic powder[16, 18, 19].

Alliin metabolism[20]

Alliin (odorless)

↓ *Allinase, activated by heat or cutting*

Allicin (garlic odor)

↙ ↘

Diallyl trisulfide	Diallylsulfides
Diallyl disulfide	Ajoenes
	Vinyldithiines

Garlic appears to enhance the synthesis of nitric oxide, which may account, in part, for some of garlic's antihypertensive and anticoagulant effects; this ability is retained in heat-treated and aged garlic products[21-25]. On the other hand, allicin and ajoene appear to inhibit inducible nitric oxide synthase in macrophages, reducing nitrite accumulation in atherosclerotic plaques and in hypoxic tissues[26-28].

In rats, aliin is well absorbed orally, reaching maximum serum concentrations within ten minutes, and is completely excreted within about six hours; allicin and vinyldithiines are absorbed more slowly, reaching peak levels between 30 and 120 minutes and persisting in the body for up to four days[29]. In rats, mice and dogs, S-allyl-cysteine is well absorbed orally (98-100%)[30]. There is a significant first pass effect in which allicin is metabolized to allyl mercaptan, ajoene and vinyldithiines[31]. Excretion occurs renally and through hepatic breakdown, fecal excretion and exhalation.

Garlic is also a rich source of highly bioavailable *selenium,* which is thought to account, in part, for garlic's antioxidant and cancer preventive effects; some growers add selenium to the soil to enhance garlic's selenium content[32-38].

Because of garlic's many medicinal uses, there are over 2500 scientific articles evaluating its health effects. The research is nicely summarized in several books:

- Heinrich P. Koch and Larry D. Lawson: *GARLIC: The Science and Therapeutic Applications of Allium sativum L and Related Species*. Williams and Wilkins, 1996.
- Darin Ingels. *Garlic and Cholesterol*. Prima Health Publications, 1999.
- Ivan A Ross. *Medicinal Plants of the World* (Chapter 3: Garlic). Humana Press, 1999

The University of Texas Center for Alternative Medicine Research on Cancer also has a web site with extensive information about garlic: http://www.sph.uth.tmc.edu/utcam/summary/garlic.htm.

Experimental Studies

Garlic: Potential Clinical Benefits

Cardiovascular: Antilipemic, antihhypertensive, anti-atherosclerotic

1) Pulmonary: none
2) Renal and electrolyte balance: none
3) Gastrointestinal/hepatic: Spasmolytic, hepatoprotective
4) Neuro-psychiatric: none
5) Endocrine: Hypoglycemic
6) Hematologic: Antithrombotic/antiplatelet
7) Rheumatologic: none
8) Reproductive: Emmenagogue/abortifacient
9) Immune modulation: Immunostimulant
10) Antimicrobial: Antiviral, antibacterial, antifungal, antiparasitic
11) Antineoplastic: Chemoprevention
12) Antioxidant: Antioxidant
13) Skin and mucus membranes: none
14) Other/miscellaneous: Anti-vampire

1. **Cardiovascular:** Antilipemic, antihhypertensive, anti-atherosclerotic: Garlic has demonstrated effects on several risk factors for atherosclerotic disease – hyperlipidemia, hypertension, and platelet aggregation (See also **Hematologic** section below.)[39-43].
   a. Antilipemic (cholesterol lowering):
      i. *In vitro data:* In rat, chicken and monkey hepatocytes, garlic paste, garlic oil, allicin and ajoene significantly reduced cholesterol biosynthesis by inhibiting HMG-CoA reductase and 14-alpha-demethylase[44-50]. Some authors postulate that garlic's trace minerals, such as tellurium, also inhibit hepatic cholesterol synthesis[51], but most

attribute garlic's antilipemic effects to diallyl disulfide, a decomposition product of allicin[12, 52].

ii. *Animal data:* Garlic lowers hyperlipidemia in animal studies[53]. In rats, both garlic protein and garlic oil exhibited significant lipid lowering effects, primarily through a decrease in hepatic cholesterogenesis[54]. Rats on an atherogenic diet were supplemented with freeze-dried garlic powder; garlic exerted a dose-effect response with the highest doses lowering serum cholesterol significantly, enhancing the ratio of HDL cholesterol to LDL cholesterol[55]. Rats given a high sucrose diet (which generally increases tissue cholesterol and triglyceride levels by 50%) who received garlic oil supplements had significant attenuation of their serum and tissue cholesterol, triglyceride and lipid levels[56].

Chickens whose diets were supplemented with garlic powder had significant reductions of plasma and tissue cholesterol and plasma triacylglycerols. Garlic supplementation also significantly decreased 3-hydroxy-3-methylglutaryl reductase activity and cholesterol 7 alpha-hydroxylase activity[57].

In several studies in rabbits fed a high cholesterol diet, garlic or allicin supplementation significantly inhibited hypercholesterolemia, decreased tissue cholesterol, lowered low density lipoprotein (LDL) concentrations, raised high density lipoprotein (HDL) concentrations, and reduced atheromatous changes in the aorta by 50%[58-66]. In another rabbit study, garlic was as effective as gemfibrozil in lowering hypercholesterolemia[67].

In rats given endothelial injuries of the carotid artery and then fed a cholesterol-rich diet, those given garlic supplementation had a significant inhibition of hypercholesterolemia; garlic also provided significant protection for the enzymes of the glutathione-dependent peroxide detoxification system, which are strongly impaired under hypercholesterolemia[68]. Similarly, in rabbits given arterial endothelial injuries and then fed a high cholesterol diet, those assigned to garlic supplements (Kyolic®) had a significant reduction in the development of fatty streaks and plaques and in-vessel-wall cholesterol accumulation, thus providing protection against the onset of atherosclerosis[69].

In another study, rats were given garlic, ginger or garlic/ginger supplements for four weeks. All groups exhibited significant decreases in blood glucose, serum total cholesterol and serum alkaline phosphatase. Cholesterol was significantly decreased in animals fed with combination of the two, compared to either alone, indicating that a combination of garlic and ginger is much more effective in reducing blood glucose and serum lipids than either herb alone[70].

iii. *Human data:* Since 1975, over 35 human studies have evaluated garlic's lipid-lowering effects[20]. Case series and controlled trials in healthy adults given garlic supplements along with cholesterol rich diets suggest that garlic can reduce mean serum cholesterol levels and increase fibrinolytic activity[71, 72]. Although the quality of randomized trials has been only modest, recent meta-analyses have concluded that in over a dozen trials published between 1979 and 1993, there was an average improvement in serum cholesterol concentrations of 9% - 12% and a significant reduction in serum triglycerides in hyperlipidemic patients taking standardized garlic powder supplements of 600–900 mg daily; the improvement was evident within one month[40, 73-87].

Subsequent randomized trials have had mixed results (with negative results often reported by studies with small sample sizes or using steam-distilled garlic oil), but tend to support garlic powder's ability to lower cholesterol concentrations modestly[88-96]. Garlic oil appears to be less efficacious than garlic powder, presumably because the oil does not contain allicin, the active ingredient in the powder[95, 97].

In a randomized, controlled trial, 50 adult men with moderate hypercholesterolemia were randomly assigned for 12 weeks to one of four groups: 1) placebo, 2) 900 mg garlic/day and 12 g oil placebo/day, 3) 900 mg placebo/day and 12 g fish oil/day, and 4) 900 mg garlic/day and 12 g fish oil/day. Garlic supplementation significantly decreased both total cholesterol and LDL-C. In patients taking both garlic and fish oil, garlic reversed fish-oil-induced increases in LDL-C[98].

In adults with intermittent claudication, supplementation with garlic powder (800 mg daily for 12 weeks) was associated with a significant improvement in serum cholesterol concentration and a clinical improvement in walking distance[99].

In a single blind, placebo-controlled crossover study, 40 hypercholesterolemic adults were assigned to either placebo for one month or fish oil (1800 mg of eicosapentanoic acid [EPA] + 1200 mg of docosahexanoic acid [DHA]) with garlic powder (1200 mg) capsules daily for one month. Supplementation with garlic resulted in an 11% decrease in cholesterol, a 34% decrease in triglycerides, and a 10% decrease in low-density lipoprotein (LDL) levels, as well as a 19% decrease in cholesterol/high-density lipoprotein (HDL) risk[100].

In a double-blind placebo controlled trial among 115 hypercholesterolemic adults assigned to a low fat, low cholesterol diet, those given 900 mg/day of dried garlic powder, standardized to 1.3% allicin, did not have any significant differences from the placebo treated group in the mean concentrations of serum lipids, lipoproteins or apo A1 or B[92]. Negative results were also noted in two other studies of hypercholesterolemic patients (N=40 and N=28) on a low fat diet who were supplemented with 900 mg daily of Kwai® garlic powder[90, 94]. These results indicate that in patients following a low-fat, low-cholesterol diet, garlic supplementation may have little additional lipid-lowering effect.

In a randomized, controlled double blind study of 152 adults, supplementation with 900 mg daily of standardized garlic powder (Kwai®) for four years reduced plaque volume in the carotid and femoral arteries by 9-18%, decreased LDL-C by 4%, increased HDL concentration by 8%, and lowered blood pressure by 7%[101].

In a controlled clinical trial, 30 patients with coronary artery disease (CAD) were administered garlic while another 30 patients received a placebo. Garlic, administered in a daily dose of four capsules (containing ethyl acetate extract from 1 g peeled and crushed raw garlic), significantly reduced total serum cholesterol and triglycerides, and significantly increased HDL-cholesterol and fibrinolytic activity[102].

In a placebo-controlled trial of 25 patients with moderate hypercholesterolemia, those assigned to a steam-distilled garlic oil preparation (5 mg twice a day) for 12 weeks did not have significantly lower serum lipoprotein levels, total cholesterol, LDL-cholesterol, HDL-C, or triglycerides[95]. This article was criticized on the basis that a garlic oil rather than garlic powder preparation was used; because garlic oil does not contain allicin, it probably has minimal impact on serum lipids.

The efficacy of a garlic-ginkgo combination product (Allium Plus®) was analyzed in a randomized, placebo-controlled, double-blind study of 43 patients with elevated total cholesterol levels ranging between 230 and 390 mg/dl. Only 20% of the patients in the placebo group showed an improvement of their total cholesterol level, whereas 35% of the treatment group did ($p < 0.05$)[103].

In a placebo-controlled trial in 35 renal transplant patients, those given garlic supplements (680 mg bid) for six weeks had a significant reduction in total serum cholesterol and LDL-cholesterol compared with placebo treated patients[104].

In a placebo-controlled randomized trial in 30 pediatric patients with familial hypercholesterolemia, eight weeks of supplementation with 900 mg daily of garlic (Kwai®) had no significant impact on fasting cholesterol levels or low density lipoproteins[105].

b. Antihypertensive

i. *In vitro data:* In isolated strips of canine carotid arteries and in isolated rat aorta, garlic exerted direct vasodilating effects[106, 107]. Garlic also activated the synthesis of nitric oxide, which is a potent endogenous vasodilator[21].

ii. *Animal data:* Garlic extracts reduce blood pressure in rats and dogs[108-111]. In anesthetized dogs, for example, gastric administration of encapsulated garlic powder induced dose-dependent natriuretic and diuretic responses which reached a maximum 30-40 minutes after garlic administration and decreased to basal levels after 100-150 minutes. A simultaneous decrease in arterial blood pressure was observed which continued past the 250-minute mark[112]. In rabbits, intravenous administration of

garlic extracts elicited a dose-dependent diuretic-natriuretic response and a gradual decrease in heart rate, but not in arterial blood pressure[113].

iii. *Human data:* In a study of 20 normal adults, garlic powder supplements significantly increased the diameter of conjunctival venules and arterioles[114].

In a meta-analysis of seven placebo-controlled clinical trials using Kwai® garlic powder supplementation, three showed a significant reduction in systolic blood pressure (SBP) and four in diastolic blood pressure (DBP). The overall pooled mean difference in the change in SBP was 5-7% greater in the subjects who were treated with garlic then in those treated with placebo. The corresponding reduction in DBP in the garlic-treated subjects was slightly smaller[77, 115]. In one of these studies, the onset of garlic's hypotensive action was within five hours after administration of a single dose of 2400 mg of dried garlic; the effect lasted more than 14 hours[116].

In a prospective, four-year clinical trial of atherosclerotic adults, standardized garlic powder supplementation (900 mg daily) lowered blood pressure by 7% ($P<0.05$)[101].

c. Anti-atherosclerotic

i. *In vitro data:* (Also see the above section on antilipemic effects, and the **Hematologic** section below.) In cell cultures, aqueous solutions of dried garlic powder containing allicin and ajoene significantly inhibited the proliferative activity of smooth muscle cells from atherosclerotic aortic plaques[117, 118].

ii. *Animal data:* In hypercholesterolemic rabbits, garlic supplements significantly reduced the aortic lesions and lipid content of existing fatty plaques[62].

iii. *Human data:* In a randomized, placebo controlled trial in ten healthy adults, there was a significant improvement in plasma viscosity and capillary blood flow within five hours after taking 900 mg of standardized garlic powder[119].

In a prospective cohort study, 101 healthy adults who took at least 300 mg daily of dried garlic powder for at least two years were compared with 101 age and gender matched controls who were not taking supplements; pulse wave velocity and elastic vascular resistance (two measures of arterial elasticity) were significantly lower in the garlic group than in the control group, even after controlling for age and

systolic blood pressure, i.e. chronic garlic powder intake was associated with an attenuation in age-related increases in aortic stiffness[120].

In a placebo-controlled trial of patients with stage II peripheral arterial occlusive disease, garlic powder supplements (800 mg daily) were associated with a significant increase in walking distance by 46 meters; the improvement started after the fifth week of treatment[99].

In a prospective, four-year clinical trial of patients treated with 900 mg daily of standardized garlic powder, there was a 9-18% reduction in plaque volume, a 4% decrease in LDL levels, an 8% increase in HDL concentrations, and a 7% decrease in blood pressure[101]. Similar results were reported in a four-year German trial in 152 older adults; those who took high dose garlic for four years reduced atherosclerotic plaque in both carotid and femoral arteries by 5-18%[121].

In a three-year-long controlled study of 432 patients who had suffered a myocardial infarction, those who were assigned to daily supplementation with freshly extracted garlic oil had a significant reduction in the rate of reinfarction (35%) and mortality (45%)[122].

2. **Pulmonary:** none
3. **Renal and electrolyte imbalance:** none
4. **Gastrointestinal/hepatic:** Spasmolytic, hepatoprotectant
   a. Spasmolytic: Although garlic has been used to calm gastrointestinal spasms, there are no studies evaluating this effect. Many persons who take high doses of garlic actually experience gastric irritation.
   b. Hepatoprotectant
      i. *In vitro data:* In rat liver cultures, garlic administration prior to exposure to hepatotoxins (such as carbon tetrachloride, galactosamine and doxorubicin) provided protection against histologic and biochemical evidence of damage[123-126].
      ii. *Animal data:* In mice, rats and chickens, pretreatment with oral garlic supplements provided significant protection against the toxicity of known hepatotoxins, including heavy metals[127-132]. In toads and rats, pretreatment with garlic protected against aflatoxin- and chemically induced liver tumors[133, 134]. Aged garlic and garlic's

diallyl sulfur compounds protected against acute chemically induced hepatotoxicity in rats[125, 126, 131].

iii. *Human data:* In one case report, a patient with severe hepatopulmonary syndrome who failed somatostatin therapy and declined liver transplantation began taking large daily doses of powdered garlic; she experienced partial palliation of her symptoms and some objective signs of improvement over 18 months of continuous self-medication[135].

5. **Neuro-psychiatric:** none
6. **Endocrine:** Hypoglycemic: Although several animal studies suggest that high doses of garlic can lower elevated blood sugars[136-143], there are no human studies suggesting that garlic has antidiabetic properties or hypoglycemic effects[106].
7. **Hematologic:** Antithrombotic/antiplatelet: Fresh garlic, garlic powder, aged garlic and garlic oil have demonstrated antiplatelet/anticoagulant effects by interfering with cyclo-oxygenase-mediated thromboxane synthesis[144-155]. Several garlic compounds contribute to this antithrombotic effect: alliin, ajoene, allicin, vinyldithiines and diallyl disulfide[144, 156]. These effects appear to be important contributors to garlic's beneficial effects in atherosclerotic conditions[157]. Although early reports implicated allicin as the primary anticoagulant, more recent studies suggest that ajoene is the most important contributor to garlic's anticoagulant effects[158-162].

   i. *In vitro data:* In rabbit platelets and lung and vascular tissues, raw garlic inhibited cyclooxygenase activity non-competitively and irreversibly; on the other hand, boiled garlic had little effect on cyclooxygenase activity[163]. In pigs' aortic endothelium, ajoene (which reversibly inhibits platelet aggregation) prevented thrombus formation both at low and high shear rates[159]. Ajoene and diallyl sulfide also inhibited prostaglandin synthetase (96%) and lipoxygenase (100%), thereby decreasing thromboxane synthesis and inflammatory cytokines[164].

   Incubation of garlic and its constituents (diallytrisulfide, 2-vinyl-1,3-dithiene, allyl 1,5-hexadienyltrisulfide) with platelets inhibited aggregation induced by ADP, epinephrine, collagen, thrombin, arachidonate, and platelet activating factor (PAF)[165]. In

six healthy adults, the essential oil of garlic inhibited *in vitro* platelet aggregation induced by ADP, epinephrine or collagen; the effect was dose-related. Oral administration of garlic also decreased platelet aggregation[166]. In another study of platelets from healthy adults who had eaten four fresh garlic cloves, there was a complete inhibition of platelet aggregation induced by 5-hydroxytryptamine[167].

Ajoene synergistically potentiated the anti-aggregatory action of prostacyclin, indomethacin and dypyridamole[168].

ii. *Animal data:* In pial microvessels of the mouse, garlic was compared with aspirin in terms of inhibition of platelet aggregation. The time for the first platelet aggregate to appear in pial arterioles was significantly delayed (P…0.001) by the 100 mg/kg garlic dose, comparable to that of the 25 and 50 mg/kg ASA doses[169].

In rabbits, an aqueous extract of garlic demonstrated a dose-dependent inhibition of thromboxane production, but there was no impact on prostacyclin synthesis[170].

In rabbits given collagen and arachidonic acid intravenously, those pretreated with an aqueous extract of garlic (500 mg/kg) exhibited significant protection from thrombocytopenia and hypotension. Thromboxane-B2 synthesis was significantly reduced in animals pretreated with garlic and then injected with a lethal dose of either collagen or arachidonic acid[171]. Garlic pretreatment also provided significant protection against experimental infusions of soluble rat tail tendon collagen (which causes thrombocytopenia, respiratory distress, seizures and death) and arachidonic acid (which also causes thrombocytopenia, indicative of *in vivo* platelet aggregation). Histopathological examination of lung and liver tissues of animals pretreated with garlic, then treated with a lethal dose of collagen or arachidonic acid, showed a significant reduction in the damage compared to animals not pretreated with garlic[127].

iii. *Human data:* In case series and randomized, controlled trials in healthy adults and in those with vascular disease, garlic supplementation (600–800 mg daily) has reduced platelet aggregation and enhanced fibrinolysis, probably by interfering with thromboxane synthesis[43, 76, 156, 172].

In a study in 14 normotensive men, garlic supplements had no significant effect on platelet aggregation or serum thromboxane concentrations[173]; however, other case

series have reported more positive effects. Among adult volunteers given one clove (approximately 3 g) of fresh garlic daily for 26 weeks, there was an approximately 80% reduction in serum thromboxane[174]. In a case series, 20 patients with ischemic heart disease were given either fried or raw garlic; fibrinolytic activity increased by 72% and 63% within six hours of administration of raw or fried garlic, respectively, and the elevated levels were maintained for up to 12 hours. After 28 days of administration, fibrinolytic activity showed a sustained increase, rising 84.8% (raw) and 72% (fried)[175]. In patients with peripheral arterial occlusive disease, 12 weeks of therapy with garlic powder (800 mg daily) decreased thrombocyte aggregation and plasma viscosity significantly[99].

In a randomized, double-blind, placebo controlled cross-over study of 12 healthy adults, dried garlic powder supplementation (900 mg daily) led to significantly higher total fibrinolytic activity and tissue plasminogen activator activity within two to four hours of garlic ingestion. Platelet aggregation was also significantly lower after seven and 14 days of garlic treatment[176]. Similarly, in a placebo-controlled clinical trial of 120 adult volunteers, those treated with 800 mg garlic powder daily for four weeks had a significant reduction in spontaneous platelet aggregation, improved plasma viscosity, decreased diastolic blood pressure and enhanced microcirculation of the skin; the effects were especially marked in the 64 patients with elevated spontaneous platelet aggregation[177].

In a ten-month study of 15 hypercholesterolemic men comparing the effect of aged garlic extract with placebo, those assigned to garlic supplementation had a significant reduction of epinephrine- and, to a lesser degree, collagen-induced platelet aggregation and a 30% reduction in platelet adhesion to fibrinogen[178]. In a double-blind, placebo-controlled study of 60 adults with cerebrovascular risk factors, those assigned to 800 mg of powdered garlic daily for four weeks had significant inhibition of spontaneous platelet aggregation and of circulating platelet aggregates[179].

8. **Rheumatologic:** none
9. **Reproductive:** Emmenagogue/abortifacient: Despite garlic's widespread traditional use as an abortifacient, there are no epidemiologic studies suggesting an association between garlic intake and miscarriage. There is one *in vitro* studies showing that garlic causes uterine stimulation when applied to rat uteri, but no reports from animal or human studies suggesting that normal dietary intake of garlic is problematic for pregnant mothers or their fetuses. In a study in rats, oral administration of alcoholic garlic extracts did NOT have any abortifacient effects[9].
10. **Immune modulation:** Immunostimulant
    i. *In vitro data:* In mouse macrophages, an aqueous garlic extract and a protein fraction isolated from the extract demonstrated significant dose-related augmentation of oxidative burst and enhanced T-lymphocyte blastogenesis[180].

       Alliin significantly increased pokeweed mitogen-induced peripheral blood mononuclear cell (PBMC) proliferation, increased IL-1-beta and TNF-alpha production, and enhanced the engulfing capacity of phagocyting cells; Con-A induced cell proliferation and IL-6 production decreased following incubation with alliin, whereas PHA-induced cell proliferation, IL-2 and superoxide anion generation remained unchanged[181].

       Aged garlic extract significantly enhanced the cytotoxicity of human peripheral blood lymphocytes (PBL) against both natural-killer (NK)-sensitive K562 and NK-resistant M14 cell lines. This effect was enhanced synergistically by concurrent treatment with interleukin 2 (IL-2), suggesting that garlic extracts serve as efficient immunostimulant[182].

    ii. *Animal data:* none

    iii. *Human data:* none
11. **Antimicrobial:** Antiviral, antibacterial, antifungal, antiparasitic. Garlic is nicknamed Russian penicillin for its widespread use as a topical and systemic antimicrobial agent[149, 183, 184]. Allicin has antimicrobial effects *in vitro* against many viruses, bacteria, fungi and parasites, but dried, powdered and oil preparations of garlic have not been shown to have significant antimicrobial activity[185].

a. Antiviral

i. *In vitro data:* Garlic and its sulfur constituents demonstrated antiviral activity against *Coxsackie virus spp, Herpes Simplex Virus types 1 & 2, Influenza B, Parainfluenza Virus type 3, Vaccinia Virus, Vesicular Stomatitis Virus, Human Immunodeficiency Virus type 1* and *Human Rhinovirus type 2*. The order for virucidal activity generally was: ajoene > allicin > allyl methyl thiosulfinate > methyl allyl thiosulfinate; no activity was found for the polar fractions, alliin, deoxyalliin, diallyl disulfide, or diallyl trisulfide[186-189]. Garlic extract exhibited a dose dependent inhibitory effect against human cytomegalovirus in tissue cultures[190].

ii. *Animal data:* Garlic supplements provided synergistic protection with influenza vaccine against influenza infections in mice[191, 192].

iii. *Human data:* Despite its widespread historical use and folklore about garlic's use in treating viral infections, there have been no reported randomized controlled trials evaluating its use as an antiviral agent or comparing it to standard pharmaceutical agents.

b. Antibacterial

i. *In vitro data:* Crude garlic extracts exhibited activity against both gram negative *(E. coli, Proteus spp, Salmonella, Serratia, Citrobacter, Enterobacter, Pseudomonas, Klebsiella)* and gram positive *(Staphylococcus aureus, Streptococcus pneumoniae, Streptococcus sanguis, Group A Streptococcus, B anthracis)* bacteria at room temperature, but there were no significant effects if the garlic had been boiled for five minutes before testing[183, 185, 193, 194, 195].

Ajoene, a garlic-derived sulfur-containing compound, demonstrated antimicrobial activity against gram-positive bacteria, such as *Bacillus cereus, Bacillus subtilis, Mycobacterium smegmatis, Streptomyces griseus, Staphylococcus aureus* and *Lactobacillus plantarum* and against gram-negative bacteria, such as *Escherichia coli, Klebsiella pneumoniae,* and *Xanthomonas maltophilia*; ajoene also inhibited yeast growth at concentrations below 20 micrograms/mL[196-198]. Allicin exerted antibacterial activity against *Salmonella typhimurium*, primarily by interfering with RNA synthesis[199].

Aged garlic extracts demonstrated dose-dependent antimicrobial activity against three different reference strains of *H. pylori* at concentrations of 2-5 mg per mL; however, heat treatment of the extracts reduced the inhibitory or bactericidal activity against *H. pylori* [200-202]. Garlic also exhibited synergistic effects against *H. pylori* when given along with a proton pump-inhibitor (omeprazole)[200, 203].

Garlic inhibited the growth of 20 different strains of *Mycobacterium avium intracellulare* isolated from AIDS patients and non-AIDS patients[204].

ii. *Animal data:* In rabbits, aqueous garlic extract and allicin had significant antibacterial activity against *Shigella flexneri*, fully curing the infected rabbits within three days compared with a mortality rate of 80% within 48 hours in the untreated rabbits; antibacterial activity against the challenge strain was observed in the sera of the treated rabbits within 30-60 min of administration of the agent[205].

In chickens given oral garlic supplements, there was a marked reduction in the viable count of gram negative fecal bacteria within 24 hours[193].

Studies conducted on the comparative action of raw garlic extract and tetracycline hydrochloride in equal concentrations showed the raw garlic extract to be a more potent antimicrobial agent than tetracycline against rats' fecal flora[206].

iii. *Human data:* In an epidemiologic survey of 241 Chinese adults from a region with a high incidence of stomach cancer who underwent gastroscopy, infection with *H. pylori* was a significant risk factor for the development of gastric lesions, gastric dysplasia and gastric cancer; garlic intake was inversely associated with *H. pylori* infection and gastric pathology[207].

A crossover trial in ten adults with *H. pylori* disease failed to find any significant inhibitory effect of one large dose (ten fresh cloves) of garlic on *H. pylori* as measured by breath testing performed immediately before and the morning after consumption[208]. In a Turkish study, 20 adults with *H. pylori* disease and dyspepsia were given 275 mg garlic oil supplements three times daily (with or without omeprazole) for two weeks; four weeks later, there was no change in *H. pylori* density or histologic findings of chronic active gastritis[209].

There are no controlled studies evaluating the antibacterial effects of garlic or comparing it with standard antibiotics in the treatment of cellullitis, otitis media or other bacterial infections.

c. Antifungal: Garlic enjoys a worldwide reputation as an antifungal folk remedy.

i. *In vitro data:* Aqueous garlic extract and concentrated garlic oil showed similar or better inhibitory effects than pharmaceutical preparations and demonstrated similar minimum inhibitory concentrations against *Aspergillus*[210]. Aqueous extract of garlic, diluted 1:150 and 1:100, inhibited 50 and 90% of dermatophytes such as *Microsporum canis, M. gypseum, M. audouinii, Trichophyton rubrum, T. mentagrophytes, T. violaceum, T. simii, T. verrucosum, T. erinacei, and Epidermophyton floccosum* as effectively as ketoconazole in concentrations of 1 and 2.5 micrograms/mL[9, 195, 211, 212]. Other studies documented that aqueous garlic extracts had fungicidal effects against *Candida, Cryptococcus, Rhodotorula, Torulopsis* and *Trichosporum*[213-215].

Allicin demonstrated fungicidal activity against numerous yeast and fungi, including *Candida albicans, Cryptococcus, Trichophyton, Histoplasma capsulatum* and *Cryptococcus neoformans*[194, 197, 216-222]. Diallyl trisulfide had antifungal activity against *C. neoformans*; it had synergistic fungicidal effects when administered with amphotericin B[223]. Its *in vitro* activity against yeast has led some herbalists and naturopaths to recommend garlic as a treatment for vaginal and systemic yeast infections[224].

A concentrated garlic extract had potent *in vitro* effects against *Cryptococcus neoformans*; it also demonstrated synergistic fungistatic effects with amphotericin B[225].

The growth of both *Aspergillus niger* and *Candida albicans* was inhibited by ajoene at concentrations less than 20 micrograms/mL[226].

ii. *Animal data:* Garlic has demonstrated antifungal effects in chicks and rabbits[227, 228].

iii. *Human data:* In a Chinese case series of 16 patients with cryptococcal meningitis who were treated with garlic alone, six were cured and five reportedly improved significantly.

After oral ingestion of 25 mL of a fresh aqueous garlic extract by adult volunteers, anticandidal and anticryptococcal activities were detected in undiluted serum 30 and 60 minutes after ingestion; no detectable antifungal activity was found in the excreted urine at any time after oral ingestion[229]. Two patients with cryptococcal meningitis were given a commercial garlic extract intravenously; plasma titers of anti-*Cyptococcus neoformans* activity rose twofold over preinfusion titers. Anti-*C. neoformans* activity was detected in four of five cerebrospinal fluid samples[230].

Among 34 soldiers with tinea pedis, treatment with a cream containing ajoene resulted in complete clinical and mycological cure in 27 (79%) after seven days of treatment. The remaining seven patients (21%) achieved complete cure after seven additional days of treatment; none had positive mycotic cultures during the 90 day follow-up[231].

In an Indian case report, culture-confirmed sporotrichosis was cured by topical garlic applications[232].

In one case report, topically applied garlic was compared with tolnaftate in the treatment of *Microsporum canis* infection of the arm; the garlic treated lesions healed in ten days, compared with four weeks to heal on the tolnaftate treated sites[233].

There are no randomized trials evaluating garlic's effectiveness in treating vaginal or systemic fungal infections in adults or children.

b. Antiparasitic: Many folks healers and herbalists world wide recommend garlic as a treatment for intestinal parasites. In some cultures, children infested with helminths are treated with enemas containing crushed garlic[234].

i. *In vitro data:* Allicin exhibits antiparasitic activity against major human intestinal parasites such as *Entamoeba histolytica, Ascaris lumbricoides* and *Giardia lamblia*[197, 235, 236].

ii. *Animal data:* A parasitologist treated a dog infected with *Ancyclostoma caninum* and a man infected with *Necator americanus* with raw garlic mixed in their food for five days; there was no apparent effect on the parasites' rate of egg production, even with garlic doses as high as 20 grams daily; however, there was a significant decrease in the number of larvae recovered from stool cultures[237].

iii. *Human data:* In a case series of ten children infected with *Hymenolepis nana* and 26 infected with *Giardia lamblia*, supplementation with garlic extracts was reported to be efficient and safe and to shorten the duration of treatment[238]. Other Chinese case series report success for patients treated with garlic for pinworms and amebiasis[3].

In a case series of Brazilian children infected with *Ascaris lumbricoides*, treatment with eight grams of garlic daily for five days proved ineffective in fighting the infection[239].

12. **Antineoplastic:** Chemoprevention: Garlic and its extracts appear to protect against DNA damage *in vitro*. In animal and epidemiologic studies, garlic is associated with a reduced risk of cancer[240-243].

i. *In vitro:* At least two anti-carcinogenic agents have been identified in garlic: diallyl sulfide and glutathione-S-transferase[244]. Garlic constituents, particularly allicin, are cytotoxic against HeLa and Vero cell lines at concentrations used to achieve anti-viral effects[187].

Ajoene induces apoptosis in human promyeloleukemic cells[245].

In B-cell lymphoma cell lines, ajoene exerted cytostatic and cytotoxic effects[246].

Pretreatment of head and neck squamous cell carcinoma cell lines with S-allyl cysteine significantly enhanced the cytotoxic effects of cisplatin, but had no cytotoxic effects when given alone[247].

In human peripheral blood lymphocytes, a water extract of raw garlic and S-allylcysteine (SAC) significantly inhibited adduct formation induced by benzo[a]pyrene (BaP); in addition, reactive oxygen species-induced 8-oxodeoxyguanosine in DNA was reduced in the presence of SAC[248].

In the glandular stomach mucosa of rats, pretreatment with diallyl sulfide significantly and dose-dependently inhibited chemically-induced nuclear aberrations and ornithine decarboxylase activity[249].

In a transformed mammary epithelial cell culture model and in the rat mammary tumor model, treatment with garlic extracts with high selenium content resulted in growth inhibition, G1 phase cell cycle arrest and apoptotic DNA double strand breaks; there was significant cancer protection with the high selenium garlic, but none with regular garlic extract[37].

Ajoene inhibited the growth of human neuroblastoma cells *in vitro*[250]

ii. *Animal data:* Garlic and its constituents inhibit the growth of implanted tumors, reduce the risk of spontaneously occurring and chemically induced tumors, and inhibit the initiation and promotion phases of carcinogenesis in animals[251].

In mice and rats, oral supplementation with fresh garlic had a significant dose-dependent effect in reducing chromosomal aberrations induced by chemical genotoxins[252-254].

In Swiss albino mice, pretreatment with oral garlic supplements significantly reduced chemically-induced carcinogenesis of the uterine cervix (23% vs. 73%, P <0.01)[255]. Similarly, oral administration of garlic supplements inhibited the development of benzo[a]pyrene (BP)-induced neoplasia and induced increased glutathione S- transferase (GST) activity in the forestomach[256]. Topical application of diallyl sulfide and diallyl disulfide significantly inhibited skin papilloma formation induced by 7,12-dimethylbenz(a)anthracene and 12,O- tetradecanoylphorbol-13-acetate, and significantly increased the rate of survival in the murine model[257].

In hamsters, oral administration of garlic extracts three times a week for 14 weeks significantly inhibited 7,12-dimethylbenz[a]anthracene (DMBA)-induced buccal pouch carcinogenesis, reduced lipid peroxidation and enhanced the levels of GSH, GPx, and GST[258].

In rats exposed to the known carcinogen 1,2-dimethylhydrazine, those given garlic supplements had a significantly reduced incidence of colon tumors; in nude mice that had been injected with colon cancer cells, garlic supplementation significantly

prolonged survival time[259]. Similarly, in mice injected with bladder cancer cells, those pre-treated with garlic had a significantly reduced tumor incidence, slower tumor growth, and increased survival when compared with animals that received the saline control[260].

In rats, garlic compounds such as diallyl disulfide, allicin, methyl propyl disulfide and propylene sulfide significantly inhibited the development of chemically induced hepatic, colon and renal tumors[261].

In mice, garlic provided significant protection against the development of chemically induced tumors[262, 263].

In rats, pretreatment with garlic powder supplements protected against mammary tumors induced by 7,12-dimethylbenz[a]anthracene (DMBA); continuous treatment, which started before DMBA and persisted for the entire duration of the study, was most effective in tumor suppression[264]. Immediate pretreatment with garlic's sulfur compounds (diallyl disulfide > diallyl sulfide > allyl methyl sulfide) was also significantly protective; selenium-rich garlic appeared to offer more protection than regular garlic[264]. Similarly, supplementation with either normal- or high-selenium garlic during either the initiation phase or post-initiation phase of mammary carcinogenesis significantly inhibited tumor development[33]. In another study in which high-selenium garlic supplements were provided during either the early or late stage of neoplastic progression, a short-term exposure to the high-selenium garlic for one month immediately following carcinogen administration was just as effective in cancer prevention as the continuous exposure regimen (five months); however, starting garlic supplements 13 weeks after carcinogen treatment (late stages of tumorigenesis) had no impact on the number of tumors or survival[34]. In a third study, supplementation with high-selenium garlic prior to exposure to a known carcinogen significantly reduced DNA damage, normalized hepatic enzymes, and increased the concentrations of glutathione S-transferase and uridine 5'-diphosphate-glucuronyltransferase in the liver and kidney, suggesting that garlic may suppress tumor development by enhancing detoxification[36].

In hamsters, garlic supplements substantially inhibited the carcinogenic effects of topically applied 7,12- dimethylbenz[a]anthracene, a known carcinogen[265].

In mice given a chronic lethal dose of cyclophosphamide (50 mg/kg) for 14 days, intraperitoneal administration of garlic substantially reduced toxicity and increased life span by more than 70%; administration of garlic extract did not interfere with the tumor-reducing activity of cyclophosphamide[132].

iii. *Human data:* Numerous epidemiologic studies suggest that diets rich in garlic are associated with reduced risks of several kinds of solid tumors[149, 207, 240, 241, 266-277]. All studies have focused on garlic as a preventive supplement rather than as a treatment for established tumors. There are no randomized controlled trials evaluating the effectiveness of garlic supplementation in the treatment of established malignancies in adults or children.

13. **Antioxidant:** Antioxidant: Whole garlic and aged garlic extract exhibit direct antioxidant effects and enhance the serum levels of two antioxidant enzymes, catylase and glutathione peroxidase[2, 278-281].

i. *In vitro data:* Garlic extract and allicin efficiently scavenged exogenously generated hydroxyl radicals in a dose dependent fashion, but their effectiveness was reduced about 10% by heating to 100 degrees C for 20 minutes[282, 283]. Other garlic constituents, such as S-allylcysteine, also demonstrated significant antioxidant effects *in vitro*[284]. The sulfur compounds found in fresh garlic appear to be nearly 1000 times more potent as antioxidants than crude, aged garlic extract[285].

Garlic (both the homogenate of 10% in physiological saline solution and its supernatant) was able to reduce the radicals generated by the Fenton reaction and trapped by phenyl-butyl-nitron for EPR measurements; also radicals present in cigarette smoke were reduced by garlic[281].

In rat liver microsomes, garlic extract prevented formation of thiobarbituric-acid-reactive substances in cell membranes during lipid peroxidation in a dose dependent fashion[286, 287].

An aqueous extract obtained from 1 mg of a garlic preparation (Kwai®) was as effective an antioxidant as 30 nmol of ascorbic acid and/or 3.6 nmol of alpha-tocopherol[280, 288].

Several garlic constituents (diallyl sulfide, diallyl disulfide [DADS], dipropyl sulfide and dipropyl disulfide) were examined for their antiperoxidant effects. DADS, but none of the other compounds, inhibited liver microsomal lipid peroxidation induced by NADPH, ascorbate and doxorubicin[124].

ii. *Animal data:* none

iii. *Human data:* In a cohort study of 31 hypercholesterolemic patients, 20 took garlic supplements for six months (900 mg daily of Kwai® tablets) and 11 did not; oxidative resistance of low density lipoproteins was not significantly different between the two groups. However, the sample size for this study may have been too small to have sufficient clinical power to exclude a Type II statistical error[289].

In a randomized, placebo-controlled cross over trial in ten volunteers who took 600 mg daily of a standardized garlic powder preparation (Kwai® tablets), garlic supplementation was associated with a significantly (34%) decreased susceptibility to lipoprotein oxidation[290].

14. **Skin and mucus membranes:** none

15. **Other/miscellaneous:** none

Toxicity and Contraindications

All herbal products carry the potential for contamination with other herbal products, pesticides, herbicides, heavy metals, *and pharmaceuticals. This is particularly concerning with imports from developing countries.*

Furthermore, allergic reactions can occur to any natural product in sensitive persons.

Allergic reactions and contact dermatitis to garlic have been reported[291-298]. Occupational asthma has been reported in garlic harvesters[299-301].

Potentially toxic compounds in garlic: None known

Acute toxicity: As is obvious to the most casual consumer, the odor of garlic may "pervade the breath and skin"[13, 84]. Garlic is on the Food and Drug Administration's Generally Recognized as Safe (GRAS) list, but is known to cause gastric irritation if taken in high doses by sensitive individuals[302]. In randomized, controlled trials, side effects in those taking garlic included heartburn, nausea, vomiting, diarrhea, flatulence, bloating, mild orthostatic hypotension, flushing, tachycardia, headache, insomnia, sweating and dizziness as well as offensive body odor[78].

Prolonged topical use (garlic compresses left in place for six hours or more) has also led to irritant burns[303-306].

In mildly diabetic rabbits fed garlic, hypoglycemic activity and an increase in serum insulin have been noted, but this effect has not been reported in normal or diabetic humans[137, 139, 141, 143, 307, 308].

Chronic toxicity: None known. Rats fed up to 2 grams/kg of aged garlic extract for five out of seven days every week for six months demonstrated no serious toxicity[309]; intraperitoneal and oral administration of high doses (5 mL/kg of pure garlic juice) led to weight loss, hepatic and pulmonary toxicity in rats[206, 310-312]. However, in one study, hypertensive rats given garlic supplements four times daily developed erratic pulses, dehydration, weight loss and lethargy[313].

In humans, daily doses of up to 60 grams of fresh garlic and 120 mg of essential oil of garlic over a period of three months did not result in any serious disorders[14].

Garlic does not exert genotoxic effects[314, 315]; in fact, it appears to provide protection against agents with known genotoxicity, embryotoxicity and carcinogenicity[133, 252, 316-320].

There is a case report of platelet dysfunction in an 87-year-old patient who chronically took 2 grams daily of garlic cloves[321].

Limitations during other illnesses *or in patients with specific organ dysfunction:* Some herbalists recommend avoiding garlic use by patients with gastric irritation or inflammation, unstable diabetes (due to potential hypoglycemic effects found in studies in rats[139]), insomnia (garlic may exacerbate it), organ transplants (due to potential immunostimulation leading to organ rejection), acute auto-immune disorders such as rheumatoid arthritis (due to potential immunostimulation) and in those who are about to have or who have recently had surgery (due to potential anticoagulant effects)[322-325]. A spontaneous spinal epidural hematoma was reported in an 87-year-old man who chronically ingested 4 cloves of garlic daily[326].

Interactions with other herbs or pharmaceuticals: No formal drug interaction studies have been performed. Because of its antithrombotic effects, it should be used cautiously by patients taking anticoagulant medications or herbs[325]; a pharmacist reported two patients who had been stabilized on warfarin whose clotting times doubled after they began taking garlic supplements[327]. Because of its mild antihypertensive effects, patients taking garlic supplements and antihypertensive medications should be monitored closely[328].

Safety during pregnancy, lactation and/or childhood: Unknown. Presumed safe when used in normal dietary amounts. Some herbalists suggest that pregnant women avoid garlic due to findings from a single study in which garlic stimulated uterine contractions *in vitro*[325]. Garlic's sulfur compounds do cross the placenta; the amniotic fluid of women who ate garlic during pregnancy could be distinguished from that of non-garlic eaters on the basis of aroma alone[329]. Nursing infants appear to prefer the taste of maternal milk and spend more time nursing when the mother has consumed garlic[330].

Typical Dosages

Provision of dosage information does NOT constitute a recommendation or endorsement, but rather indicates the range of doses commonly used.

Doses are given for single herb use and must be adjusted when using herbs in combinations. Doses may also vary according to the type and severity of the condition treated and individual patient conditions.

There is enormous variation (30–40 fold) in the quantities of various garlic constituents in different products; garlic harvested in China may contain twice as much allicin as garlic grown in Europe or the United States[18, 106, 331]. One study compared 16 different garlic products. The best garlic powder tablets (only five brands) were equally as active as fresh cloves, but steam-distilled oils were 35% as active and oil-macerates only 12% as active[97, 332-334]. Many garlic powder products contained so little allicin as to be designated of "placebo" value only[20]. For steam-distilled oils, most of the activity was due to diallyl trisulfide. For the oil-macerates, most of the activity was due largely to the vinyldithiines. Ajoene, found in the oil-macerates, had highest specific activity but a low concentration, yielding only 13% of the activity of diallyl trisulfide and 3% of the activity of allicin[151].

In general, garlic powder contains primarily alliin and allicin; oil-macerated garlic contains mostly vinyldithiines; and steam-distilled garlic contains diallyl disulfide and other sulfides[1].

The European Scientific Cooperative on Phytotherapy recommends the daily equivalent of 6-10 mg of alliin (or 3-5 mg of allicin), which can be found in one clove of fresh garlic or in 500-1000 mg of garlic powder[14].

Examples of typical adult dosages[12, 13]:

Raw garlic cloves: 0.5-2 raw cloves (2-6 grams), up to three times daily. NOTE: One clove is approximately equivalent to 3 grams of fresh garlic.

Garlic pills standardized to 0.5% to 1.3% alliin: 600-900 mg daily divided into three doses.

Garlic powder: 0.4–1.2 grams daily divided into three doses.

Oil extract of garlic (contains no allicin or aliin, but does contain ajoene and vinyldithiines): 1-2 capsules daily or 0.03-0.12 mL TID

Juice: 2-4 mL TID

Syrup: 2-8 mL TID

Tincture (1:5, 45% alcohol): 2-4 mL TID

According to research from the Center for Science in the Public Interest, the "best buy" in terms of getting the most allicin for one's money (other than eating fresh, raw garlic) comes from buying garlic powder off the spice cabinet and putting 1/3 tsp into a gelatin capsule oneself[335].

Pediatric dosages: Unknown

Availability of standardized preparations: Yes

Proprietary products containing garlic: Sapec; A Vogel Capsules a L'Ail, Beni-cur, Carisano, Centrum Garlic, Cirkulin, Coreplex capsules, Garlimega, Ilja Rogoff, Kneipp Knoblauch Dragees N, Kneipp Knoblauch-Pflanzensaft, Kwai, Kwai N, Kyolic Aged Garlic Extract, Macro Garlic, One a Day Garlic Softgels, One a Day Cholesterol Health, Past Ail, Sapec, Sirmia Knoblauchsaft N, Strongus, Thirial

Kyolic® is an aged garlic extract that lacks allicin, but tends to cause very little gastric irritation. It effectively lowered cholesterol in at least one randomized trial and protected against atherosclerosis in animal studies[69, 93].

Kwai® is the brand most often used in clinical studies; it contains garlic powder standardized for alliin content. Nine hundred mg of Kwai is approximately equivalent to 2.7 grams of garlic.

Multi-ingredient preparations containing garlic: Allium Plus, Antifect, Arterase, Asgoviscum N, Asgoviscum Forte, Bleib Junger, Bleib Junger S, Brewers Yeast with Garlic, Buttercup Pol'N'Count, Cold-Eeze, Crataegus Complex, Discmigon, Dynamol, Echinacea & Antioxidants, Echinacea ACE Plus Zinc, Esten, Ex'ail, Garlic Allium Complex, Garlic and Horseradish + C Complex, Garlic and Horseradish Complex 1000, Gartech, Gelovitall, Ginkovit, Hanoartin, Herbal Cold & Flu Relief, Horse Radish and Garlic Tablets, Keli-Med, Kincare, Kneipp Drei-Pflanzen-Dragees, Kreislauf-Kapseln, Lifesystem Herbal Formula 7 Liver Tonic, Liver Tonic Herbal Formula 6, Macro C + Garlic with Zinc, Manns Knoblauch Pillen Plus, Odourless Garlic, Omegacelle, One a

Day Cholesterol Health, Prexene, Procold, Proesten, Protol, Proyeast, Silybum Complex, System 3-4-3 Metabolic Cleansing System, Tisane Pour le Coeur et la Circulation "H", Vitalyt

Dosages used in herbal combinations: Variable

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