Garlic consists of various dosage forms of the fresh or carefully dried bulbs of *Allium sativum*. In the U.S. and Western Europe, most of garlic’s popularity is based on the extensive traditional use of this herb, and on scientific research suggesting that cardiovascular benefits are associated with ingesting garlic as a conventional food and a dietary supplement. More than 3,000 scientific articles have been published on the chemistry, pharmacology, toxicology, and clinical uses of garlic.

**Primary Uses**
- Hyperlipidemia
- Atherosclerosis

**Other Potential Uses**
- Hypertension, mild
- Peripheral arterial occlusive disease (PAOD)
- Decreased platelet function
- Colon cancer prevention
- Stomach cancer prevention
- Coughs, colds, catarrh, and rhinitis (These traditional uses are not supported by clinical trials.)

**Pharmacological Actions**
Garlic reduces total cholesterol and serum triglycerides; elevates high density lipoproteins (HDL); prevents platelet aggregation and thrombus formation; stimulates fibrinolysis; prolongs clotting time; reduces low-density lipoprotein oxidation; reduces systolic and diastolic blood pressure; attenuates age- and blood pressure-related increases in aortic stiffness; has immunomodulating activity; reduces blood glucose levels; is antifungal and fungistatic against *Cryptococcus neoformans*; antioxidant; anti-cancer; antimicrobial; inhibits anion transport and sickle cell dehydration and restricts dense cell formation in sickle cell patients.

**Dosage and Administration**
For the prevention of atherosclerosis and prophylaxis and treatment of peripheral arterial vascular diseases, long-term treatment is generally advised. Epidemiological findings support long-term, consistent use to aid in preventing stomach and intestinal cancers.

- **Fresh Herb**: 4 g (1 clove) minced bulb daily.
- **Infusion**: 4 g in 150 ml of hot water.
- **Fluid Extract**: 4 ml [1:1 (g/ml)].
- **Tincture**: 20 ml [1:5 (g/ml)].
- **Garlic Powder (standardized)**: 200–300 mg, 3 times daily.
- **AGE™ Aged Garlic Extract (standardized)**: 300–800 mg, 3 times daily, or 1–5 ml daily.

**Contraindications**
None known according to the German Commission E and other European scientific bodies. According to the World Health Organization, patients with a known allergy to garlic and those taking warfarin (and presumably other anticoagulants) should use caution in ingesting garlic. However, a clinical trial on a proprietary aged garlic extract (AGE) showed no prolonged bleeding in patients taking warfarin. Reports of increased clotting time suggest that patients avoid garlic at least one week prior to surgery.

**Pregnancy and Lactation**: There are no restrictions on using garlic during pregnancy and lactation. A controlled trial showed that garlic’s major sulfur-containing volatile compounds are transmitted to human milk, leading to infants’ improved drinking habits.

**Adverse Effects**
Garlic odor may permeate the breath and skin. Gastrointestinal symptoms and intestinal flora changes or allergic reactions are rare. In separate single case reports, excessive ingestion of garlic was associated with postoperative bleeding, spontaneous spinal epidural hematoma, and platelet dysfunction. Occupational exposure to crushed garlic products and the topical application of garlic to treat wounds or infections may cause allergic contact dermatitis. For garlic and various generic garlic preparations, reported allergic reactions included burns, zosteriform dermatitis, induction of pemphigus (blisters), allergic asthma and rhinitis, contact urticaria, and protein contact dermatitis; but no adverse effects were reported for AGE according to toxicological and clinical studies. Garlic preparations can increase clotting time, which is sometimes beneficial, but in some cases can contribute to an adverse event. Cross-sensitivity may occur with onions and tulips.

**Drug Interactions**
 Concurrent use of garlic and antiplatelet agents (e.g., aspirin) and anticoagulants (e.g., warfarin) might increase the potential for prolonged bleeding. One report showed that clotting time doubled for 2 patients taking warfarin and garlic simultaneously, although there was insufficient information to properly assess these cases. A controlled trial on AGE resulted in no interaction with warfarin. A small trial suggests possible serum reduction of saquinavir, an anti-HIV drug.
Clinical Review

Of 32 studies (45,694 total participants) on garlic’s impact on cardiovascular and arterial health, cancer, immunity, and circulation, all but four demonstrated positive effects.

Two reviews concluded that garlic preparations might have small, positive, short-term effects (< 3 months) on lipids and promising antithrombic effects. Insignificant effects on blood pressure and no effect on glucose levels were observed. However, data was insufficient to draw conclusions about certain clinical cardiovascular outcomes (e.g. myocardial infarction), antithrombic activity, or cancer prevention. Due to the marginal quality and short duration of many trials and the unpredictable release and inadequate definition of active constituents of many garlic preparations used in the studies, conclusions regarding clinical significance are limited.

Lipid-lowering effect

Thirteen trials (795 participants) demonstrated a positive correlation between lipid-lowering effects and garlic oil, powder, or capsules. Six randomized, double-blind, placebo-controlled (R, DB, PC) studies and four DB studies supported garlic use in treating elevated lipid conditions including hyperlipidemia and hypercholesterolemia. One R, open, parallel group, comparison (O, PG, Cm) study (70 participants) found garlic powder to have a significant impact over garlic oil in lowering blood-lipid counts and blood pressure and in increasing a sense of overall well-being. An R, PC study involving 35 renal transplant patients found a garlic product to have positive effects on hyperlipidemia. One O study (82 participants) found a positive impact of garlic on coronary heart disease, in addition to its lipid-lowering effects.

A meta-analysis on garlic’s effect on total serum cholesterol levels found a statistically significant reduction in total cholesterol levels. Another study assessed and subsequently reassessed clinical data from 952 patients and 16 trials and found that all data demonstrated a significant reduction of total cholesterol when comparing garlic to placebo. Three studies on the allicin-standardized garlic powder tablets failed to show a significant reduction in elevated serum cholesterol. It was later determined that allicin released from the tablets varied significantly, and that the lack of expected allicin release possibly led to negative results. A study of 24 brands of enteric-coated tablets found that 83% of the brands released less than 15% of their allicin potential. Subsequently, the researchers recommended that manufacturers standardize supplements to dissolution of allicin release, not to allicin potential. (For non-allicin products, e.g., AGE, the standardization is to bioavailable compounds, e.g., S-allylcysteine [SAC].) In the most recent and comprehensive meta-analysis (13 R, DB, PC trials), researchers showed a significant difference (p<0.01; 5.8%) in the reduction of total cholesterol levels between baseline and placebo. The authors concluded that current evidence indicates that any specific lipid-lowering effect is small, and the clinical outcome may not be meaningful; however, there were several problems identified with the meta-analysis, indicating that conclusions can only be applied to the specific brands tested and not to the general effectiveness of garlic.

Antihypertensive effect

Two R, DB, PC studies and one R, O, PG, Cm study (159 total participants) showed garlic’s antihypertensive effects. A systematic review and meta-analysis of 8 R, C trials (415 participants) was conducted to determine garlic’s effect on blood pressure. Of the 7 trials that compared garlic with placebo, 3 demonstrated a significant reduction in systolic blood pressure (SBP), and 4 in diastolic blood pressure (DBP). The authors concluded that more rigorously designed trials might provide evidence to recommend hypertension treatment with garlic.

Antiplatelet effects

One R, DB, PC, crossover (CO) study and 2 DB, PC studies (214 total participants) indicate the potential use of garlic as a coronary disease preventative due to its positive impact on platelet functions.

Anti-atherosclerotic effect

Garlic’s positive influence on arterial and fibrinolytic activities was shown in two studies (354 participants). The longest clinical trial on garlic to date, a R, DB, PC, 4-year study (152 participants), showed that garlic had an anti-atherosclerotic impact, decreasing age-related arterial plaque. In one epidemiological, cross-sectional, observational (E, CS, OB) study (202 participants), standardized garlic powder was found to have positive effects on arterial activities, including elastic vascular resistance, pulse wave velocity, and systolic blood pressure.

Anticancer/Chemoprevention

Anti-cancer and chemopreventative qualities of garlic were shown in 5 studies (44,044 subjects). One E study of 15 years demonstrated that stomach cancer incidents were reduced with use of raw and cooked garlic. Two E studies (42,325 subjects) found that garlic intake significantly decreased colon cancer risks. Two OB studies demonstrated garlic’s chemopreventative potential through the improvement of arachidonic acid and acetaminophen metabolism. A meta-analysis of E studies on the association between garlic consumption and risk of stomach, colon, head and neck, lung, breast, and prostate cancers concluded that raw and cooked garlic use might have a protective effect against stomach and colorectal cancers.

Other

One pilot study involving 7 HIV+ patients demonstrated a positive impact on natural killer cell activity and improvement in conditions such as diarrhea, genital herpes, and candidiasis. One R, DB, PC study showed that garlic did not negatively impact bleeding potential in warfarin therapy patients. Garlic’s impact on peripheral circulation was observed in two studies: one R, CO, Cm study showed immediate improvement in hand and foot circulation; and one DB, PC study showed a significant increase in walking distance in persons with peripheral arterial occlusive disease (PAOD). The latter was the only study to meet the Cochrane Library’s inclusion criteria for its review on garlic use for PAOD. Because the one study reviewed was small, of short duration (12 weeks), and found no significant overall improvement in patients with PAOD, the Cochrane Review disagreed with the author’s findings and concluded that further trials on garlic’s effects on PAOD are warranted.
Garlic

*Allium sativum* L.  
[Fam. Liliaceae]

**Overview**
In the U.S. and Western Europe, garlic is one of the most popular substances used to reduce various risks associated with heart disease. Most of garlic’s popularity is based on the herb’s well-known folk uses and scientific research on the benefits of garlic for heart health. These health-promoting benefits may be experienced by using garlic as both a food ingredient and a dietary supplement.

**Uses**
For slightly reducing elevated levels of cholesterol in the blood; prevention of hardening of the arteries; improvement of blood flow; mild hypertension (high blood pressure); possible prevention of stomach and colon cancer; supportive therapy for peripheral arterial occlusive disease (PAOD, poor circulation to the legs causing tightness and pain in the calves when walking).

**Dosage**
Long-term treatment is generally advised in the prevention of atherosclerosis and in the prevention and treatment of peripheral arterial vascular diseases. Epidemiological findings (population studies) support long-term, consistent use for the possible prevention of stomach and intestinal cancers.

- **FRESH, MINCED GARLIC:** 1 clove daily.
- **INFUSION:** 1 clove in 150 ml of hot water.
- **GARLIC POWDER** (standardized): 200–300 mg, 3 times daily (in pill or tablet form).
- **AGE™ AGED GARLIC EXTRACT** (standardized): 300–800 mg, 3 times daily or 1–5 ml daily (in capsules).

**Contraindications**
None known according to the German Commission E and other leading scientific bodies. According to the World Health Organization, patients with a known allergy to garlic and those taking anticoagulant drugs like warfarin (Coumadin®) should be cautious about ingesting garlic. Garlic should not be taken prior to surgery (at least one week) as it may interfere with blood clotting.

**Pregnancy and Lactation:**
There are no known restrictions during pregnancy or lactation. However, some of garlic’s properties are transmitted to human milk, leading to improved drinking habits in infants.

**Adverse Effects**
Being a commonly used food, garlic is relatively safe. Adverse effects are rare, but there may be gastrointestinal symptoms and changes to the intestinal flora (beneficial bacteria that aid in digestion). Allergic reactions have been reported for garlic and various generic preparations, but no adverse effects were reported for AGE according to toxicological and clinical studies. According to one report, garlic was associated with unusual bleeding after an operation. Garlic preparations can increase clotting time, which is sometimes beneficial, but in some cases can contribute to an adverse event. Also, garlic may produce a characteristic odor on the breath or skin.

**Drug Interactions**
Taking garlic with antiplatelet agents, like aspirin, and anticoagulants, like warfarin, may increase the potential for prolonged bleeding.

Comments
When using a dietary supplement, purchase it from a reliable source. For best results, use the same brand of product throughout the period of use. As with all medications and dietary supplements, please inform your healthcare provider of all herbs and medications you are taking. Interactions may occur between medications and herbs or even among different herbs when taken at the same time. Treat your herbal supplement with care by taking it as directed, storing it as advised on the label, and keeping it out of the reach of children and pets. Consult your healthcare provider with any questions.
Garlic
Allium sativum L.
[Fam. Lilaceae]

OVERVIEW
In the United States and Western Europe, garlic is one of the most popular substances used to reduce various risks associated with cardiovascular disease. Most of garlic’s popularity is based on the extensive traditional use of this herb and on scientific research suggesting that cardiovascular benefits are associated with ingesting garlic as both a conventional food and dietary supplement (Blumenthal et al., 2000). Garlic preparations have been one of the top-selling herbal supplements on the U.S. market for many years (Brevoort, 1998), ranking third in retail sales in the mainstream market in 2000, and generating revenues over $61 million (Blumenthal, 2001). To date more than 3,000 scientific papers have been published investigating the activities of garlic and garlic compounds, including chemical, toxicological, pharmacological, clinical, and epidemiological studies (Amagase et al., 2001). Garlic preparations with uniquely different chemical compositions, including powdered dried garlic products standardized to allicin yield and aged garlic extract (AGE™) products that are standardized to S-allylcysteine (SAC), have been the subject of numerous clinical studies. Determining which forms are the most effective remains controversial and is an ongoing subject of study and debate. Medical literature includes positive outcomes in clinical studies involving several types of garlic preparations.

DESCRIPTION
Garlic preparations consist of the fresh or dried bulbs (main bulb and secondary bulbs or cloves) of Allium sativum L. [Fam. Lilaceae], and various dosage forms (Blumenthal et al., 1998). Garlic oil is not present in fresh or dried garlic bulbs; instead, the oil is produced by converting water-soluble thiosulfinates to oil-soluble sulfides via steam distillation. Aged garlic involves long-term extraction in dilute ethanol for up to 20 months, then drying; pickling garlic involves immersion in vinegar (5% acetic acid) (Amagase et al., 2001; Lawson, 1998a).

PRIMARY USES
Cardiovascular
- Hyperlipidemia (Isaacsohn et al., 1998; Lash et al., 1998; McGriddle et al., 1998; Steiner et al., 1996a, 1996b; Yeh et al., 1995; De A Santos and Johns, 1995; Steiner and Lin, 1994; Jain et al., 1993; Grünwald et al., 1992; Holzgarter et al., 1992; Mader, 1990; Vorberg et al., 1990; Lau et al., 1987; Bordia, 1981)
- Atherosclerosis (Koscielny et al., 1999)

OTHER POTENTIAL USES
Cardiovascular
- Hypertension, mild (Steiner et al., 1996; Auer et al., 1990)
- Peripheral arterial occlusive disease (PAOD) (Koscielny et al., 1999; ESCOP, 1997; Kiesewetter et al., 1993b)

Hematology
- Decreased platelet function (Rahman and Billington, 2000; Steiner et al., 2001; Steiner et al., 1996; Kiesewetter et al., 1991; Kiesewetter et al., 1993a)

Chemopreventative
- Colon cancer preventative (Steinmetz et al., 1994; Witte et al., 1996)
- Stomach cancer preventative (You et al., 1989)

Miscellaneous
- Garlic has traditionally been used to relieve cough, colds, catarrh, and rhinitis, although clinical trials do not support such uses (ESCOP, 1997)

DOSEAGE
Internal
Crude Preparations
FRESH HERB: 4 g daily (1 clove) minced bulb or equivalent preparations (Blumenthal et al., 1998). [NOTE: Some authors have suggested that this dosage level should be revised downward to approximately 2,700 mg of fresh garlic, equivalent to the 900 mg of garlic powder used in some clinical trials that studied the ability of garlic to prevent and/or reverse atherosclerotic plaque build-up (Schulz et al., 2001).]
INFUSION: 4 g in 150 ml of hot water (Blumenthal et al., 2000).
FLUID EXTRACT: 1:1 (g/ml), 4 ml (Blumenthal et al., 2000).
TINCTURE: 1:5 (g/ml), 20 ml (Blumenthal et al., 2000).

Standardized Preparations
GARLIC POWDER (Kwai®): 200–300 mg, 3 times daily (Warshafsky et al., 1993).
AGE™ (Kyolic®) aged garlic extract: 300–800 mg, 3 times daily or 1–5 ml daily (Steiner 2001; Steiner et al., 1996; Rahman and Billington, 2000; USP, 2002; Lau et al., 1987).
DURATION OF ADMINISTRATION
Long-term treatment is generally advised in the prevention of atherosclerosis (Koscienly et al., 1999), and the prophylaxis and treatment of peripheral arterial vascular diseases (ESCOP, 1997). Epidemiological observations support the long-term consistent use for prevention of cancer in the stomach and intestines (You et al., 1989).

CHEMISTRY

Crude Preparations
Fresh garlic bulbs contain about 65% water, 28% carbohydrates (fructans), 2.3% organosulfur compounds (OSC), 2% protein, and 1.2% free amino acids. The main OSC in whole garlic are the cysteine sulfoxides (1% allin and 0.1% cycloalliin) and the γ-glutamylcysteines (0.6% γ-glutamyl-S-trans-1-propenylcysteine and 0.4% γ-glutamyl-S-allylcysteine). When the bulb is bruised, crushed, chewed, or minced, the allin, in the presence of the enzyme allinase, is converted to allicin (ESCOP, 1997). One mg of allin produces 0.458 mg of allicin, which is considered to be responsible for some of garlic's biological activity and is a precursor to some thiosulfanes, which also have been shown to be active (Lawson 1998a; Block, 1985; Bradley, 1992; Budavari, 1996; ESCOP, 1997). However, allicin is unstable and decomposes to other volatile sulfur compounds (the half-life of allicin is not more than 24 hours), so the extent of allicin's activity has been questioned. Intact garlic cloves (the sections that comprise the garlic bulb) also contain S-allylcysteine (SAC), but no allicin. SAC is formed from gamma-glutamyl cysteine catabolism and has been reported to contribute to the health benefits of some garlic preparations (Amagase et al., 2001). Fresh and aged garlic extract (AGE, see below) also contain steroidal saponins (Matsuura, 2001).

Standardized Preparations
Processed garlic preparations contain a variety of sulfur-containing compounds other than those found naturally in intact garlic cloves, depending on the conditions applied (Lawson, 1998a; Fenwick and Henley, 1985). Sulfur-containing compounds in commercial garlic preparations vary, depending on their manufacturing process. Powdered preparations of dried garlic contain alliin and compounds derived from its subsequent transformation, but no allicin. Enteric coatings protect these powdered preparations from conversion while in the stomach. Garlic oil yields neither allin, nor allicin as the converting enzyme is destroyed by heat. It does contain diallyl disulfide, diallyl trisulfide, and allyl methyl trisulfide. Macerated garlic-derived oil contains vindilithiins, ajoene, and diallyl trisulfides (Lawson, 1998a). Garlic extract and odorless AGE are listed in the United States Pharmacopeial/National Formulary (USP, 2002). The most abundant sulfur compound in AGE is SAC; it is standardized to not less than 0.05% SAC (USP, 2002).

PHARMACOLOGICAL ACTIONS

Human
Garlic reduces total cholesterol (TC) and serum triglycerides (TG) and elevates high density lipoproteins (HDL) (Auer et al., 1990; Barrie et al., 1987; Lau et al., 1987; Bordia, 1981; De A Santos and Johns, 1995; Silagy and Neil, 1994a); prevents platelet aggregation and thrombus formation (Rahman and Billington, 2000; Barrie et al., 1987; Kiesewetter et al., 1993a; Kiesewetter et al., 1993b; Legnani et al., 1993); stimulates fibrinolysis, prolongs clotting time (Chutani and Bordia, 1981; Gadkari and Joshi, 1991; Harenberg et al., 1988; Legnani et al., 1993); reduces low-density lipoprotein (LDL) oxidation (Ide and Lau, 2001; Lau, 2001; Munday, 1999; Steiner and Lin, 1994; Harris et al., 1995; Phelps and Harris, 1993); reduces systolic blood pressure, diastolic blood pressure, and mean blood pressure from baseline (Steiner et al., 1996a, 1996b; De A Santos and Johns, 1995; Silagy and Neil, 1994b; Grünwald et al., 1992; Auer et al., 1990); attenuates age- and blood pressure-related increases in aortic stiffness (Breithaupt-Gröger et al., 1997); stimulates peripheral microcirculation (Okuhara, 1994); is antifungal and fungistatic against Cryptococcus neoformans, the organism that causes cryptococcal meningitis (Anon., 1980; Davis et al., 1990); may decrease the risk of gastrointestinal cancers (Gail et al., 1998; You et al., 1991, 1989, 1988; Reuter et al., 1996; Buiatti et al., 1989; Lau, 1989); modulates immune system activity (Brosche and Platt, 1993; Kandil et al., 1988; Lawson, 1998a; Reuter et al., 1996); reduces blood glucose levels (Kiesewetter et al., 1991). Garlic does not inhibit H. pylori bacteria in the stomach (Graham et al., 1999). Although one study concluded that garlic extracts had no statistically significant impact on how far patients with peripheral vascular disease (PVD) can walk (Kiesewetter et al., 1993b), AGE has been reported to exhibit stimulation of peripheral circulation in human subjects (Okuhara, 1994; Kikuchi et al., 1994). One pilot clinical trial (Ohnishi et al., 2000) indicated an effect of AGE and other antioxidants in the potential treatment of sickle cell anemia patients.

Animal
Garlic lowers elevated levels of serum homocysteine (Yeh, 1999); lowers serum cholesterol and lipids (Bordia et al., 1975; Kamanna and Chandrasekhar, 1982; Chi et al., 1982); is antithrombotic (Bordia et al., 1975); increases fibrinolysis and clotting time (Bordia et al., 1975; Reuter et al., 1996); reduces blood pressure (Sial and Ahmad, 1982; Ruffin and Hunter, 1983); is an antioxidant (Han et al., 1992; Lawson, 1998a); modulates immune system (Kyo et al., 1999, 1998; Lawson, 1998a; Reuter et al., 1996); reduces blood glucose levels and increases insulin levels (Augusti, 1975; Chang and Johnson, 1980); is anti-allergenic (Kyo et al., 1997); exhibits antitumor activity against transitional cell carcinoma of the bladder with AGE (Lau et al., 1986; Riggs et al., 1997); reduces breast cancer incidence (Amagase and Milter, 1993; Liu et al., 1992; Kröning, 1964); decreases incidence of hepatic tumors in the Bufo regularis toad (El-Mofry et al., 1994).

In vitro Antithrombotic
The rational clinical application of garlic necessitates demonstrating the association between garlic consumption and important clinical outcomes such as atherosclerosis. In vivo and in vitro studies suggest garlic extracts and several garlic constituents have a significant antithrombotic effect (Ariga et al., 1981; Boullin, 1981; Srivastava, 1986; Mohammed and Woodward, 1986). Garlic has been shown to increase fibrinolysis and prolong clotting time (Reuter et al., 1996). Adenosine in AGE and its constituents are the most potent antiplatelet constituents of garlic. Allicin was thought an active compound in garlic due to its high-reaction and oxidative characteristics, but it is rapidly metabolized in human blood (in vitro culture) and therefore might not contribute to the in vivo antithrombotic effect of garlic (Freeman and Kodera, 1995; Koch and Lawson, 1996).

Ajoene is found in small amounts in garlic oil-macerates, but not in commercial garlic preparations and garlic powders.
Bioavailability of ajoene has not yet been established. Antithrombotic and vasodilatory actions of garlic might be due to adenosine deaminase and cyclic AMP phosphodiesterase, which can be found in garlic extracts. The decrease of thromboxane B2 (TXB2) levels is another possible explanation for garlic’s antithrombotic effects. Most of the above explanations are based on in vitro and in vivo experiments (Berthold and Sudhop, 1998; Rahman and Billington, 2000; Bordia et al., 1996; Agarwal 1996).

Koscielny et al. (1999) reported a slowing and reversal of atherosclerotic plaque formation. AGE has been shown to protect vascular endothelial cells against hydrogen peroxide-induced lipid peroxidation and biomembrane damage (Yamasaki et al., 1994); prevent oxidized LDL-induced membrane damage, loss of cell viability, and lipid peroxidation (Ide and Lau, 1997b); and demonstrate antihypertensive activity (Lawson, 1998a; Steinet et al., 1996; Koch et al., 1992a; Sendi et al., 1992).

Anticancer
Garlic inhibits the induction and growth of cancer (Milner, 1996; Lea, 1996). The effect on tumor initiation and promotion has been documented, and both the oil-soluble and water-soluble OSCs such as methyl propyl disulfide and propylene sulfide, SAC, S-allylmercaptocysteine (SAMC), and allicin reduce the proliferation of neoplasms and inhibit the development of liver glutathione S-transferase placental (GST-P) positive tumor foci and other indications of cancer in different organs. In contrast, OSCs such as diallyl sulfide, diallyl trisulfide, and allyl methyl trisulfide enhance the formation of liver tumor foci. However, in rats, diallyl disulfide shows the following activities: inhibits the potential for colon and renal tumor development (Fukushima et al., 1997); inhibits the growth of human prostate cancer cells (Pinto et al., 1997a); demonstrates cytotoxic activity against MBT2 bladder tumor cells (Riggs et al., 1997); is antiallergenic (Kyo et al., 1997); stimulates macrophage activity, natural killer cells, and LAK cells. It may also increase production of interleukin (IL-2), tumor necrosis factor (TNF) and interferon gamma, which are cytokines associated with beneficial antitumor responses. AGE protects against the immunosuppression induced by chemo- and radiation therapy (Lamm and Riggs, 2000; Lau, 1989) and UV light (Reeve et al., 1993a, 1993b).

Antimicrobial effects
Antibacterial activity against Escherichia, Salmonella, Staphylococcus, Streptococcus, Klebsiella, Proteus, Bacillus, Mycobacterium, Clostridium, and resistant strains (Adetumbi and Lau, 1983; Farbman et al., 1993; Hughes and Lawson, 1991; Lawson 1998a; Reuter et al., 1996); antifungal activity against Candida and Cryptococcus (Annon., 1980; Caporaso et al., 1983; Hughes and Lawson, 1991; Lawson, 1998a); antiulcer/antibacterial against Helicobacter pylori (Sivam, 2001; Sivam et al., 1997); antifungal, antiparasitic (Ankri and Mirelman, 1999). The main antimicrobial effect of allicin is limited when in direct exposure to the microorganisms due to its chemical reaction with enzymes (e.g., alcohol dehydrogenase, thioredoxin reductase) and RNA polymerase. This reaction can affect the essential metabolism of cysteine proteinase activity involved in the virulence of Entamoeba histolytica. An aqueous extract of garlic cloves, standardized for its thiosulfinate concentration tested positively for its antimicrobial activity against H. pylori (Sivam et al., 1997). Minimum inhibitory concentration was 40 mcg thiosulfinate per ml. It is possible that the sensitivity of H. pylori to garlic extract at such low concentrations may be related to the reported low risk of stomach cancer in those populations with high allium vegetable intake. However, an uncontrolled trial involving 20 patients with positive urea breath tests, taking 300 mg tablets of dried garlic powder, three times daily for eight weeks, did not eradicate H. pylori (Fennerty et al., 1999).

Hematology effects
In vitro studies (and a pilot clinical trial) have indicated an effect of AGE and other antioxidants in the potential treatment of sickle cell anemia patients (Ohnishi et al., 2000, 2001; Ohnishi and Ohnishi, 2001).

MECHANISM OF ACTION

Lipid-lowering
- One possible mechanism is thought to be attributed to allicin/thiosulfinates (Lawson, 1998a; Reuter et al., 1996) but a recent study revealed water-soluble OSC, e.g., SAC and SPC, may be the active compounds inhibiting cholesterol synthesis (Liu and Yeh, 2001). However, oil-soluble OSC, e.g., diallyl disulfide (DADS) and others, decomposed from thiosulfinates including allicin, actually killed the cells, thus indirectly inhibiting cholesterol synthesis (Liu and Yeh, 2001).
- Increases catabolism of fatty acid-containing lipids, especially triglycerides (Yeh et al., 1995; Yeh and Yeh, 1994; Lawson, 1998a).
- Inhibits cholesterol biosynthesis at the level of β-hydroxy-β-methylglutaryl-CoA (HMG-CoA) reductase (Yeh et al., 1995; Yeh and Yeh, 1994; Gebhardt et al., 1994; Gebhardt, 1993).
- Inhibits cholesterol biosynthesis at later steps, as evidenced by accumulation of the cholesterol precursors, lanosterol and 7-dehydrocholesterol, although this latter effect may be of minor therapeutic significance (Gebhardt et al., 1994; Gebhardt, 1993).
- Enhances palmitate-induced inhibition of cholesterol biosynthesis (Gebhardt, 1995).
- Inhibits cholesterol biosynthesis by targeting squalene monoxygenase, an enzyme that catalyzes the downstream pathway in cholesterol synthesis (in vitro study on fresh garlic extract) (Gupta and Porter, 2001).
- Lipid-lowering activity may be due to the presence of steroid saponins in fresh garlic and AGE, which may interfere with the absorption of total and LDL cholesterol from the intestine lumen, thereby reducing plasma levels (40–57% in test animals), without adversely affecting HDL levels. Saponins are known to inhibit intestinal absorption of cholesterol, suggesting possible hypocholesterolemic effect (Matsuura, 2001).

Antithrombotic
Garlic inhibits platelet aggregation and stimulates fibrinolysis; this may be attributed to allicin/thiosulfinates at lower garlic doses and cycloallin at higher garlic doses (in vitro) (Lawson, 1998a; Reuter et al., 1996). However, since it is argued that allicin/thiosulfinates may not be bioavailable, other compounds may be responsible (Amagase et al., 2001).
- Inhibits normal arachidonate metabolism (Ariga et al., 1981; Makheja et al., 1980; Makheja et al., 1981; Reuter et al., 1996).
• Inhibits the lipoxygenase and cyclo-oxygenase pathways of the arachidonic acid cascade, thereby inhibiting the synthesis of prostaglandins and thromboxanes (PGE2, PGD2, PG12, TXB2) (Rahman and Billington, 2000; Reuter et al., 1996; Ariga et al., 1981; Makheja et al., 1981, 1980).

• Inhibits fatty acid lipoxygenase (Liu and Yeh, 2001; Reuter et al., 1996; Ariga et al., 1981; Makheja et al., 1981, 1980).

• Ajoene affects fibrinogen-induced human platelet aggregation and inhibits binding of fibrinogen to adenosine diphosphate (ADP) stimulated platelets in vitro (Reuter et al., 1996).

Antimicrobial

• Action is thought to be attributed to γ-glutamylcysteines and fructans; allicin is not involved (Lawson, 1998a; Reuter et al., 1996).

• γ-Glutamylcysteines can inhibit angiotensin-converting enzyme (ACE), thus inhibiting angiotensin II (a hormone that increases vasoconstriction) (Lawson, 1998a; Sendel et al., 1992).

• Fructans can inhibit adenosine deaminase in isolated cells, thus increasing adenosine and its associated blood vessel dilatory activity (Lawson 1998a; Koch et al., 1992).

• Increases nitric oxide through activation of nitric oxide synthase activity (Das et al., 1995).

Antimicrobial

• Action is in vitro or externally thought to be attributed to allicin/thiosulfonates (Lawson, 1998a; Reuter et al., 1996).

• Allicin disrupts cellular metabolic processes in vitro through inactivation of proteins by oxidation of essential thiols to disulfide, competitive inhibition of enzymes containing cysteine in their active sites by reacting with the sulfhydryl (-SH) group, and noncompetitive inhibition of enzymes by reacting with -SH groups at allosteric sites (Adetumbi and Lau, 1983; Cavallito et al., 1944; Lawson, 1998a).

• Garlic extract inhibits H. pylori bacterial in vitro at moderate concentrations, thereby suggesting mechanism for antigastric ulcer effect (Sivam, 2001; Sivam et al., 1997).

Anticancer

• Action is thought to be attributed to any number of garlic compounds: SAC, SAMC, thiosulfonates, γ-glutamylcysteines, and other unknown compounds (Lawson, 1998a; Pinto et al., 1997b; Reuter et al., 1996, Amagase and Milner, 1993; Liu et al., 1992) although the thiosulfonates (e.g., allicin) are questioned due to their instability.

• Decreases the amount of nitrate-reducing bacteria in the stomach, thus reducing the formation of carcinogenic nitrosamines (Dion and Milner, 1996; Mei et al., 1985, 1982).

• Inhibits the induction and growth of cancer, which may be mediated by modulation of carcinogen metabolism (Lea, 1996).

• Stimulates macrophage activity, natural killer cells, and LAK cells, and might increase the production of IL-2, TNF, and interferon gamma, which are cytokines associated with beneficial antitumor response (Lamm and Riggs, 2000; Lau et al., 1991; Lau, 1989; Abdullah et al., 1989).

Antiallergenic

• Inhibits antigen-specific histamine release from mast cells in vitro (Kyo et al., 1997); decreases antigen-specific IgE mediated skin reactions in vivo (Kyo et al., 1997); and reduces antigen-specific, late-phase reaction by modulating the production and release of cytokines from activated T-lymphocytes in vivo (Kyo et al., 1997).

Antioxidant

• Action is thought to be attributed to primarily watersoluble OSC (e.g., SAC and SAMC) in addition to fructosyl-arginine, other Maillard reaction compounds in AGE, and other compounds (Ryu, 2001; Imai, 1994); some authors suggest action may be due to the allicin/thiosulfonates (Lawson, 1998a; Reuter et al., 1996).

• Decreases oxidation of LDL cholesterol in humans (Ide and Lau, 2001; Lau, 2001; Munday, 1999; Steiner and Lin, 1994; Harris et al., 1995; Phelps and Harris, 1993).

• Increases the activity of several enzymes (including glutathione peroxidase and catalase) involved in antioxidative processes and decreases the concentration of lipid peroxides in the blood (Ide and Lau, 1999; Steiner and Lin, 1994; Geng and Lau, 1997; Han et al., 1992).

• Increases intracellular glutathione (GSH) (a potent intracellular antioxidant and detoxifier), modulates the activity of the GSH redox cycle, and increases activity of superoxide dismutase (SOD, a potent intracellular antioxidant) activity (Ike and Lau, 2001; Wang et al., 1999; Hatono et al., 1996; Geng and Lau, 1997).

Immunomodulatory

• Action thought to be attributed to protein fraction of garlic (Moraika et al., 1993; Lau et al., 1991; Hirao et al., 1987).

• Inhibits activation of nuclear factor kappa B (NF-κB) in human T-cells that are involved in immune and inflammatory reactions (Geng et al., 1997).

• Increases phagocytosis, natural killer cell activity, antibody titer, and lymphocyte counts (Brosche and Platt, 1993; Kandil et al., 1988; Lawson, 1998a; Reuter et al., 1996).

Hematological (AGE)

• Inhibits anion transport and sickle cell dehydration (Ohnishi et al., 2001); restricts dense cell formation (Ohnishi and Ohnishi, 2001) and 4.0 mg/mL was shown to inhibit dense cell formation by 50% (Ohnishi et al., 2000). A U.S. patent has been granted to Wakunaga of America, Mission Viejo, CA for the “Therapeutic Uses of Specially Processed Garlic for Sickle Cell Disease” (Ohnishi and Tsuyoshi, 2001).

• Increased natural killer cell activity and improved helper suppressor T-cell ratios in AIDS patients (Abdullah et al., 1989).

CONTRAINDICATIONS

None known according to the German Commission E and other leading European scientific bodies (Blumenthal et al., 1998; ESCOP, 1997). The World Health Organization (WHO) cautions against the use of garlic by patients with a known allergy to garlic, and those taking warfarin (and presumably other anticoagulants) (WHO, 1999). However, AGE has been tested in a placebo-controlled, double-blind clinical trial in patients taking Coumadin® (warfarin); there was no demonstrated interaction
with Coumadin® and no prolonged bleeding (Rozenfeld et al., 2000). Several case reports of increased clotting time suggest that patients should discontinue use prior to surgery (Brinker, 2001), usually by at least one week.

**PREGNANCY AND LACTATION:** None known (Blumenthal et al., 1998; ESCOP, 1997). A controlled trial showed that major sulfur-containing volatiles from garlic are transmitted to breast milk, leading to improved drinking habits of infants (ESCOP, 1997; Mennella and Beauchamp, 1991). In Japan, AGE is an ingredient in pharmaceutical products that are used in nutritional nourishment for pregnant and lactating women.

**ADVERSE EFFECTS**

The most commonly reported adverse effect of garlic is that its odor may pervade the breath and skin (Blumenthal et al., 1998). Raw garlic has a stronger odor and higher levels of high molecular weight sulfur compounds than cooked garlic, but malodorous breath tested in humans who ingested raw garlic showed higher levels of low molecular weight sulfur compounds and different constituents than those associated with common halitosis (Tamaki and Sonoki, 1999). Differences in the frequency of other adverse effects caused by various garlic preparations have not been completely determined (Mulrow et al., 2000), such adverse effects being dependent upon the method of preparation. Gastrointestinal symptoms and changes to the intestinal flora or allergic reactions are rare but are occasionally reported (Lembo et al., 1991). In separate, single-case reports, garlic was associated with postoperative bleeding (Burnham, 1995), spontaneous spinal epidural hematoma, and platelet dysfunction from excessive ingestion (Rose et al., 1990). Occupational exposure to crushed garlic products and the topical application of garlic to treat wounds or skin infections may cause allergic contact dermatitis (Lee and Lam, 1991; Bojs and Svensson, 1998). Allergic reactions including burns (Roberge et al., 1997), zosteriform dermatitis (Farrell and Staughton, 1996), induction of pemphigus (blisters) (Brenner and Wolf, 1994), allergic asthma and rhinitis, contact urticaria, and protein contact dermatitis have been reported for garlic and various generic garlic preparations (WHO, 1999; DeSmet, 1992), but no adverse effects were reported for AGE according to toxicological and clinical studies (Miyoshi et al., 1984; Nakagawa et al., 1984, 1980; Sumiyoshi et al., 1984). Cross-sensitivity may occur with onions and tulips (Siegers, 1992; WHO, 1999). Garlic preparations can increase clotting time (Chutani and Bordia, 1981; Gadkari and Joshi, 1991; Harenberg et al., 1988; Legnani et al., 1993), which is sometimes beneficial, but in some cases, can contribute to an adverse event.

**DRUG INTERACTIONS**

Concurrent use of garlic and antiplatelet agents (e.g., aspirin) and anticoagulants (e.g., warfarin) might increase the potential for prolonged bleeding. One report showed that clotting time (International Normalization Ratio) doubled for two patients taking warfarin and garlic simultaneously (Sunter, 1991); however, this report lacks adequate data to assess causality (Rotblatt and Ziment, 2001). Further, a controlled clinical trial on AGE showed no interactions with warfarin (Rozenfeld, 2000). Another trial on nine HIV-negative individuals produced significant decreases in serum levels of the anti-HIV drug saquinavir (Piscitelli et al., 2002); however, this study has design problems rendering the results uninterpretable.

**AMERICAN HERBAL PRODUCTS ASSOCIATION (AHPA) SAFETY RATING**

**CLASS 2C:** Not to be used while nursing (McGuffin et al., 1997). However, a controlled trial indicated a positive therapeutic use during lactation (ESCOP 1997; Mennella and Beauchamp, 1991).

**REGULATORY STATUS**

**CANADA:** Drug or possibly “New Drug” if claims made. Food in absence of claims (HPB, 1993). Schedule OTC “Herbal and Natural Products” and “Homeopathic Products” have marketing authorization with Drug Identification Numbers (DIN) assigned (Health Canada, 2001).

**EUROPEAN UNION:** Powder, freeze-dried, or low temperature dried (<65°C), containing not less than 0.45% allicin, official in European Pharmacopoeia 3rd ed. Suppl. 2001 (Ph.Eur., 2001).

**FRANCE:** Traditional Herbal Medicine (THM) permitted for treatment of minor circulatory disorders (Bradley, 1992). Essential oil is dispensed as an aromatherapy drug (Goetz, 1999).

**GERMANY:** Fresh or carefully dried bulb is approved by Commission E as non-prescription drug (Blumenthal et al., 1998). Fresh bulb for preparation of mother tincture official in the German Homoeopathic Pharmacopoeia (GHP, 1993).

**GHANA:** Monograph for fresh whole bulb occurs in Ghana Herbal Pharmacopoeia (GHP, 1992).

**INDIA:** Bulb and oil are approved single drugs dispensed in Unani system of medicine (CCRUM, 1997).

**JAPAN:** OTC drug for fatigue (Okada and Miyagaki, 1983). AGE approved for nourishment of pregnant and lactating women.

**SWEDEN:** Classified as ‘Natural Remedy’ for self-medication requiring pre-marketing authorization from Medical Products Agency (MPA). One product (e.g. Bio-Garlic Pharma Nord) is listed in the “Authorised Natural Remedies” with the approved indication “Traditionally used for the relief of cold symptoms” (MPA, 2001a; Tunón, 1999). Homeopathic dilutions (e.g., Radiotron AB) are also registered drugs (MPA, 2001b).

**SWITZERLAND:** Powdered garlic in tablets, standardized powdered extract in tablets, oily macerate in capsules, and multiple-herb preparations containing standardized garlic extract have positive classification (List D) by the Interkantonale Kontrollstelle für Heilmittel (IKS) and corresponding sales category D, with sales limited to pharmacies and drugstores, without prescription (Morant and Ruppanner, 2001). Twenty-eight garlic phytomedicines and two homeopathic medicines are listed in the Swiss Codex 2000/01 (Ruppanner and Schaefer, 2000).

**U.K.:** Herbal medicine on the General Sale List (GSL), Table A (internal or external use), Schedule 1 (requires full product license) (GSL, 1989).

**U.S.:** Dietary Supplement (USC, 1994). Fresh or dried compound bulbs, powdered garlic, fluidextract and extract are official in the U.S. National Formulary 19th edition (USP, 2002). Tincture of mature bulb, 1:10 (w/v) in 55% alcohol (v/v), is a Class C OTC drug of the Homoeopathic Pharmacopoeia of the United States (HPUS, 1989).
Clinical Review
Thirty-two studies, including 45,694 participants, are outlined in the following table, “Clinical Studies on Garlic.” All but four of the studies (Berthold et al., 1998; Issaehoh et al., 1998; McCrindle et al., 1998; Simons et al., 1995) demonstrated positive effects on conditions including cardiovascular and arterial health, cancer, immunity, and circulation. Studies from the table are categorized and discussed in the following six sections. In addition to the studies in the table, this Clinical Review discusses numerous reviews and meta-analyses that are not listed in the table.

Based on the Agency for Healthcare Research and Quality’s (AHRQ) review and summary of clinical studies on garlic (Mulrow et al., 2000), researchers concluded that garlic preparations may have small, positive, short-term effects (less than three months) on lipids, and promising antithrombotic effects. However, the data was insufficient to draw conclusions about certain clinical cardiovascular outcomes (e.g., myocardial infarction), antithrombotic activity, or cancer prevention. No effects on glucose or insulin sensitivity, or consistent decreases in blood pressure were found. Case-control studies suggest that consuming large amounts of garlic in the diet may reduce the risks of laryngeal, gastric, colorectal, and endometrial cancers, and adenomatous colorectal polyps (Mulrow et al., 2000). A subsequent review of 45 randomized trials by some of the same researchers concluded that the trials suggest possible small short-term benefits of garlic preparations on some lipid and antiplatelet factors, insignificant effects on blood pressure, and no effect on glucose levels (Ackermann et al., 2001). Conclusions regarding clinical significance are limited due to the marginal quality and short duration of many trials, as well as the unpredictable release and inadequate definition of active constituents in many of the garlic preparations used in the studies.

Lipid-lowering effect
Thirteen trials involving a total of 795 participants demonstrated a positive correlation between garlic oil, powder, or capsule intake and lipid-lowering effects. Six randomized, double-blind, placebo-controlled (R, DB, PC) studies (Yeoh et al., 1995; Jain et al., 1993; Rotzsch et al., 1992; Auer et al., 1990; Mader et al., 1990; Vorberg et al., 1990), as well as two DB, multi-center studies (Grünwald et al., 1992; Holzgartner et al., 1992) supported the use of garlic in treating elevated lipid conditions including hyperlipidemia and hypercholesterolemia. Three studies showed the positive impact of taking Kyolic® capsules specifically for improving hypercholesterolemia conditions (Steiner et al., 1996; Steiner and Lin, 1994; Lau et al., 1987). One R, open, parallel group, comparison (O, PG, Cm) found garlic powder to have a significant impact over garlic oil on lowering blood lipid counts and blood pressure, as well as increasing the overall sense of well-being in 70 subjects (De A Santos and Johns, 1995). An R, PC study involving 35 renal transplant patients found the garlic product, Pure-Gar®, to have positive effects on hyperlipidemia (Lash et al., 1998). One O study involving 82 subjects (Bordia, 1981) found garlic to have, in conjunction with the lipid-lowering effects, a positive impact on patients with coronary heart disease.

A meta-analysis of the effect of garlic on total serum cholesterol levels found a statistically significant reduction in total cholesterol levels (Warshafsky et al., 1993). Another analysis assessed clinical data from 952 patients and 16 trials, indicating a decrease in total cholesterol levels (Silagy and Neil, 1994b). A subsequent reanalysis of all data still demonstrated a significant reduction of total cholesterol compared to placebo (Warshafsky et al., 1993). Three studies on the allicin-standardized garlic powder tablets (Kwai®) failed to show a significant reduction in elevated serum cholesterol (Isaacsohn et al., 1998; McCrindle et al., 1998; Simons et al., 1995). It was later determined that the allicin release from the tablets varied significantly, and that negative studies were possibly due to the lack of expected allicin release (Lawson et al., 2001). A study of 24 brands of enteric-coated tablets found that 83% of the brands released less than 15% of their allicin potential (Lawson and Wang, 2001). Therefore, the researchers recommend that manufacturers standardize supplements to dissolution of allicin release, not to allicin potential. (For non-allicin releasing products, e.g., AGE, the standardization is to other compounds, e.g., SAC.) In a recent, comprehensive meta-analysis of 13 R, DB, PC trials researchers demonstrated a significant difference (p<0.01) in the reduction of total cholesterol levels between baseline and placebo, equivalent to a 5.8% reduction in total cholesterol levels. The authors concluded that current evidence indicates that any specific lipid-lowering effect is small, and the clinical outcome may not be meaningful (Stevinson et al., 2000). However, there were several problems identified with the meta-analysis, indicating that the conclusions can only be attributed to the specific brands tested and not the effectiveness of garlic in general. In particular, the brand used in 10 of the trials did not protect alliinase from exposure to gastric acid. Another tested supplement was spray-dried, resulting in the loss of alliin. The study on the garlic oil that showed no effect utilized a form that has demonstrated low bioavailability; therefore the conclusions of the meta-analysis need to be considered within this context (Lawson, 2001). Several of these products are not standardized to a bioavailable marker compound. Clinical studies with positive outcomes using AGE standardized with bioavailable SAC have shown significant levels of SAC in human blood during the study period (Steiner and Li, 2001).

Antihypertensive effect
Two R, DB, PC studies and one R, O, PG, Cm study (159 total participants) demonstrated the antihypertensive effects of garlic (De A Santos and Johns, 1995; Jain et al., 1993; Auer et al., 1990). A systematic review and meta-analysis of randomized controlled trials was conducted to determine the effect of garlic on blood pressure. Eight trials, including 415 participants, were identified. Of the seven trials that compared the effect of garlic with a placebo, three demonstrated a significant reduction in systolic blood pressure (SBP), and 4 in diastolic blood pressure (DBP). The authors concluded that more rigorously designed trials can provide evidence to recommend the clinical application of garlic in the treatment of hypertension (Silagy and Neil, 1994b).

Antiplatelet effects
One R, DB, PC, crossover (CO) study and 2 DB, PC, studies involving a total of 214 subjects indicate the potential use of garlic as a coronary disease preventative due to its positive impact on platelet functions (Steiner and Li, 2001; Kiesewetter et al., 1991; 1993a).

Anti-atherosclerotic effect
In the longest clinical trial on garlic to date, garlic’s ability to prevent and possibly reverse atherosclerosis was tested in a R, DB, PC, four-year study in which 152 men and women were given 900 mg garlic powder as tablets (Kwai®) per day (Koscielny et al., 1999). The subjects possessed significant plaque buildup and at least one additional cardiovascular risk factor (e.g., high LDL
levels, hypertension, diabetes, and/or history of smoking). After the four years, garlic subjects had an average 2.6% reduction in plaque volume while the placebo group's plaque increased 15.6%. Researchers concluded that garlic has a preventive and possibly curative role in arteriosclerosis therapy. In one epidemiological, cross-sectional, observational (E, CS, OB) study with 202 participants, standardized garlic powered was found to have positive effects on arterial activities including elastic vascular resistance, pulse wave velocity, and systolic blood pressure (Breithaupt-Groger, 1997).

**Anticancer/Chemoprevention**

Anti-cancer and chemopreventative qualities of garlic were demonstrated in five studies involving a total of 44,044 subjects. One E study spanning over a period of 15 years, demonstrated that raw and cooked garlic use had a significant impact on decreasing stomach cancer incidents (You et al., 1989). Two other E studies found that garlic intake significantly decreased the risk of colon cancer in 42,325 participants (Witte et al., 1993b; Steinmetz et al., 1994). Garlic's chemopreventative potential was demonstrated in two OB studies through the improvement of arachidonic acid and acetaminophen metabolism (Dimitrov and Bennink, 1997; Gwilt et al., 1994). Case-control studies suggest that consuming large amounts of garlic in the diet may reduce the risks of laryngeal, gastric, colorectal, and endometrial cancers and adenomatous colorectal polyps (Mulrow, et al., 2000).

Several reviews of E studies have examined the cancer-preventive effect of garlic, including garlic ingested as a food (Dorant et al., 1993; Fleischauer et al., 2000). A meta-analysis of the epidemiological evidence on the association between garlic consumption and risk of stomach, colon, head and neck, lung, breast, and prostate cancers concluded that raw and cooked garlic consumption might have a protective effect against stomach and colorectal cancers (Fleischauer et al., 2000). An earlier review of in vitro, in vivo, epidemiologic, and case-control studies suggested that the evidence is not conclusive to support chemoprevention in humans, but further research is warranted (Dorant et al., 1993); however, this review preceded much of the salient research in this area.

**Other**

One pilot study involving 7 HIV+ patients demonstrated a positive impact on natural killer cell activity as well as improvement in conditions such as diarrhea, genital herpetic, and candidiasis (Abdullah et al., 1989). One R, DB, PC study showed that garlic did not negatively impact bleeding potential in patients undergoing warfarin therapy (Rozenfeld, et al., 2000). Two studies involving 92 subjects demonstrated garlic's positive impact on peripheral circulation: one R, CO, Cm study showed an immediate improvement in hand and foot circulation (Okuhara, 1994); and one DB, PC study involving 80 subjects with peripheral arterial occlusive disease (PAOD) showed a significant increase in walking distance (Kiesewetter et al., 1993b). This last study was the only study to meet the inclusion criteria established by the Cochrane Library for its review on the use of garlic for PAOD. The Cochrane Review concluded that further trials on garlic's effectiveness on PAOD are warranted because the one study reviewed was small, of short duration (12 weeks), and found no significant overall improvement in patients with PAOD. The discrepancy between the conclusions of the study and those of the review is a result of the study's analysis of the mean difference between the garlic and placebo groups instead of analyzing the mean change within the groups' pre- and post-treatment.

**BRANDED PRODUCTS**

AGE™ (Aged Garlic Extract): Wakunaga of America Co., Ltd. / 23501 Madero / Mission Viejo, CA 92691 / U.S.A. / Tel: (800) 421-2998 / www.kyolic.com. This refers to a proprietary garlic extract with stable sulfure compounds standardized to bioavailable components (e.g., SAC) in various types of formulations. See Kyolic® below.

Höfel's® Garlic Pearles One-A-Day: Seven Seas Ltd., a division of the Merck Group / Hedon Road / Marfleet / Hull / England / HU9 5N] / U.K. / Tel: +44-1482-37-5234 / Fax: +44-1482-37-4345 / Email: info@hofels.com or Info@Seven-Seas Ltd.uk / www.hofels.com. A gelatin or gelatin capsule containing 2 mg garlic oil, and soybean oil.


Kwai®N LI 111: Lichtwehr Pharma AG. One tablet contains 100 mg dried powder from *Allium sativum* (garlic bulb) standardized to contain 1.3% allicin (yielding 0.6% allicin). Inactive ingredients: lactose, magnesium stearate, powdered cellulose, colloidal anhydrous silica, methylhydroxypropylcellulose, polyethylene glycol 6000, castor oil, talc, polyvinylpyrrolidone 25, sucrose, gelatin, quinoline yellow E 104, indigotine E 132, carnauba wax, cera alba.

Kyolic® Liquid: Wakunaga of America Co., Ltd. Aged Garlic Extract™ in water and residual alcohol from extraction.

Kyolic® Reserve: Wakunaga of America Co., Ltd. 600 mg Aged Garlic Extract™ per capsule.

Kyolic® Super Formula 100: Wakunaga of America Co., Ltd. 300 mg Aged Garlic Extract™ per capsule plus whey.

Kyolic® Super Formula 101: Wakunaga of America Co., Ltd. 270 mg Aged Garlic Extract™ per capsule, plus brewer's yeast, kelp, and whey.

Kyolic® Super Formula 102: Wakunaga of America Co., Ltd. 350 mg Aged Garlic Extract™ per capsule, plus food enzymes: amylase, protease, lipase, and cellulase (30 mg).

Kyolic® Super Formula 103: Wakunaga of America Co., Ltd. 220 mg Aged Garlic Extract™ per capsule, plus Ester C® (105 mg), Astragalus membranaceous (100 mg), and calcium (23 mg).

Kyolic® Super Formula 104: Wakunaga of America Co., Ltd. 300 mg Aged Garlic Extract™ per capsule, plus 190 mg lecithin.

Kyolic® Super Formula 105: Wakunaga of America Co., Ltd. 200 mg Aged Garlic Extract™ per capsule, plus beta-carotene (6 mg), vitamin C (120 mg), vitamin E (60 IU), selenium (25 mg), and green tea (45 mg).

Kyolic® Super Formula 106: Wakunaga of America Co., Ltd. 300 mg Aged Garlic Extract™ per capsule, plus saw palmetto berry (50 mg), cayenne pepper (10 mg), and vitamin E (100 IU).

Pure-Gar® Garlic Powder A-2000: Essentially Pure Ingredients™, c/o Pure Gar L.P. / 21411 Prairie Street / Chatsworth, CA 91311 / U.S.A. / Tel: (800) 537-7695 /
www.essentiallypure.com. Dried powder from Allium sativum (garlic bulb): allicin yield 2,000 ppm min.; total thiolsulfates yield 2,100 ppm minimum; allian 7,500 ppm minimum; gamma-glutamylcysteines 10,000 ppm minimum.

Pure-Gar® Garlic Powder A-5000: Essentially Pure Ingredients™ / 21411 Prairie Street / Chatsworth, CA 91311 / U.S.A. / Tel: 818-739-6046 / www.essentiallypure.com. Dried powder from Allium sativum (garlic bulb): allicin yield 5,000 ppm minimum; total thiolsulfates yield 5,000 ppm minimum; allian 11,000 ppm minimum; gamma-glutamylcysteines 10,000 ppm minimum; total sulfur 6,500 ppm minimum.

Pure-Gar® Garlic Powder A-8000: Essentially Pure Ingredients™. Dried powder from Allium sativum (garlic bulb): allicin yield 8,000 ppm minimum; total thiolsulfates yield 8,000 ppm minimum; allian 18,000 ppm minimum; gamma-glutamylcysteines 8,000 ppm minimum.

Pure-Gar® Garlic Powder A-10000: Essentially Pure Ingredients™. Dried powder from Allium sativum (garlic bulb): allicin yield 10,000 ppm minimum; total thiolsulfates yield 10,000 ppm minimum; allian 23,000 ppm minimum; gamma-glutamylcysteines 8,000 ppm minimum.

*American equivalents, if any, are found in the Product Table beginning on page 398.

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USC. See: United States Congress.


WHO. See: World Health Organization.


### Cardiovascular Hyperlipidemia/Hypercholesterolemia/Hypertension/Related Risk Factors

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Subject</th>
<th>Design</th>
<th>Duration</th>
<th>Dosage</th>
<th>Preparation</th>
<th>Results/Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berthold et al., 1998</td>
<td>Hypercholesterolemia (mean TC 291 mg/dl and mean LDL 207 mg/dl)</td>
<td>R, DB, PG n=25 (diet not controlled)</td>
<td>12 weeks</td>
<td>5 mg, 2x/day or placebo (with meals)</td>
<td>Tegra® garlic oil (oil bound to b-cyclodextrin for slow release)</td>
<td>The garlic preparation did not influence serum lipoproteins, cholesterol, absorption, or cholesterol synthesis. Garlic oil could not be recommended for hypercholesterolemia. The study was criticized for slow-release aspect that has been found to greatly reduce total absorption and because the oil preparation contained a different chemical profile than preparations used in other studies.</td>
</tr>
<tr>
<td>Isaacsohn, Lash, McCrindle, 1996</td>
<td>Hyperlipidemia (LDL&lt;160 mg/dl; TG &lt;350 mg/dl)</td>
<td>R, PC, PG, MC n=50 (n=28 taking garlic; n=22 taking placebo) subjects on the NCEP Step I diet 8 weeks before and during treatment</td>
<td>12 weeks</td>
<td>300 mg, 3x/day</td>
<td>Sapec®, Kwai® garlic powder</td>
<td>No significant lipid or lipoprotein changes between the two groups. Compliance to diet was same for both groups; however, effect of diet on lipid/lipoprotein levels prior to treatment may have influenced treatment. Another factor possibly influencing the results is the alleged change made to the tablets’ enteric coating in 1992–1993 (Lawson, 1998).</td>
</tr>
<tr>
<td>Lash et al., 1998</td>
<td>Hyperlipidemia in renal transplant patients (TC&gt;185 mg/dl; LDL&gt;160 mg/dl)</td>
<td>R, PC n=35 (garlic n=19; placebo n=16) (NCEP Step I diet during treatment)</td>
<td>12 weeks</td>
<td>680 mg, 2x/day</td>
<td>Pure-Gar®</td>
<td>At 6 weeks, there was a significant decrease from baseline of 14 mg/dL in TC (p&lt;0.05) and 12 mg/dL in LDL (p&lt;0.05). Authors noted that although garlic showed benefit, patients still required drug therapy to treat hyperlipidemia. They suggested that garlic may be used to decrease the required dosage of HMG-CoA reductase inhibitors.</td>
</tr>
<tr>
<td>McCrindle et al., 1998</td>
<td>Hypercholesterolemia in children (TC&gt;185 mg/dl)</td>
<td>R, DB, PC n=30 (garlic n=15; placebo n=15) NCEP Step 2 diet for 6 months prior to treatment</td>
<td>8 weeks</td>
<td>300 mg, 3x/day</td>
<td>Kwai® garlic powder</td>
<td>There was no significant reduction attributed to garlic for cardiovascular risk factors, with the exception of a small increase in apolipoprotein A-I levels. Authors note that adult studies have yielded positive results.</td>
</tr>
<tr>
<td>Steiner et al., 1996</td>
<td>Hypercholesterolemia (men) (TC=220–280 mg/dL)</td>
<td>DB, PC, C n=41</td>
<td>6 months, crossed over for 4 months (placed on NCEP Step I diet 4 weeks prior to washout throughout)</td>
<td>3 capsules</td>
<td>Kyolic® AGE capsules vs. placebo capsules</td>
<td>Total cholesterol (TC) levels were reduced 6.1–7% compared to placebo period or baseline (p&lt;0.0001), respectively. No difference noted for total glycerides (TG) or HDL (p=0.004). LDL decreased 4% and systolic blood pressure (SBP) decreased 5.5% (p=0.0001) with the garlic and modes decreased in diastolic blood pressure (DBP). Authors concluded AGE garlic supplementation has beneficial effects on lipid profile and BP in moderately hypercholesterolemic patients.</td>
</tr>
<tr>
<td>Yeh et al., 1995</td>
<td>Hypercholesterolemia (TC=220–285 mg/dL)</td>
<td>DB, PC, R n=34 (garlic n=17; placebo n=17) men (35–55 years old)</td>
<td>5 months</td>
<td>3 capsules</td>
<td>Kyolic® AGE capsules vs. placebo capsules containing common food ingredient</td>
<td>At 4th and 5th month, TC levels in AGE group 6% and 7% lower, respectively than baseline value and no change in placebo group. Plasma HDL-cholesterol and triglyceride levels not altered by AGE or placebo. Compared with placebo LDL-cholesterol level significantly lower in AGE group (145 ± 25 vs. 165 ± 24 mg/dL). AGE supplementation has significant mild cholesterol lowering effect in hypercholesterolemic men.</td>
</tr>
<tr>
<td>De A Santos and Johns, 1995</td>
<td>Garlic powder vs. garlic oil on blood lipids, blood pressure, and well-being</td>
<td>R, O, PG, Cm, n=70 (garlic powder n=36; or garlic oil n=34)</td>
<td>16 weeks</td>
<td>200 mg, 3x/day</td>
<td>Garlic powder: Kwai® (tablet), Garlic oil: Hofes® Original Garlic Oil Capsules</td>
<td>Lipid-lowering effect for garlic powder=11% vs. 3% for oil. LDL lowered by 16% vs. 1% respectively. HDL did not change significantly and TG did not change. Also noted was a decrease in blood pressure with garlic powder but not for oil. Well-being assessment improved for powder but not for oil. Garlic powder appears to be superior to oil in reducing cholesterol, BP, and improved well-being.</td>
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</table>

### Cardiovascular (cont.)

#### Hyperlipidemia/Hypercholesterolemia/Hypertension/Related Risk Factors (cont.)

<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Subject</th>
<th>Design</th>
<th>Duration</th>
<th>Dosage</th>
<th>Preparation</th>
<th>Results/Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simons et al., 1995</td>
<td>Hypercholesterolemia (mild to moderate) (5.5–8.0 mmol/L)</td>
<td>R, DB, PC, CO n=28</td>
<td>12 weeks after 28 day baseline dietary period; 28 day washout at end</td>
<td>300 mg, 3x/day</td>
<td>Kwai® garlic powder</td>
<td>No demonstrable effect of garlic on oxidizability of LDL on ratio of plasma lathosterol/cholesterol (a measure of cholesterol synthesis), nor on LDL cholesterol but no change in HDL cholesterol; no significant reductions in measured platelet adhesion (34–58%) and aggregation (10–25%). Study suggests AGE supplementation has beneficial effects on lipids, especially platelets, that may lead to cardiovascular risk reduction.</td>
</tr>
<tr>
<td>Steiner and Lin, 1994</td>
<td>Hypercholesterolemia (TC=210–290 mg/dL)</td>
<td>DB, CO, R n=45 men (30–70 years old)</td>
<td>10 months</td>
<td>700 mg, 3 capsules, 3x/day</td>
<td>Kyolic® AGE capsules vs. placebo capsules</td>
<td>66% of subjects in garlic group showed modest reduction (about 8%) of total and LDL cholesterol but no change in HDL cholesterol. No change in HDL cholesterol but no significant reductions in measured platelet adhesion (34–58%) and aggregation (10–25%). Study suggests AGE supplementation has beneficial effects on lipids, especially platelets, that may lead to cardiovascular risk reduction.</td>
</tr>
<tr>
<td>Jain et al., 1993</td>
<td>Serum lipids, lipoproteins, glucose, and blood pressure</td>
<td>R, DB, PC n=42</td>
<td>12 weeks</td>
<td>300 mg, 3x/day or placebo</td>
<td>Garlic powder in tablet form</td>
<td>Experimental group experienced a 6% reduction in TC (p&lt;0.01) vs. placebo group (1%) reduction. LDL decreased 11% and 3% respectively (p&lt;0.05). No changes in HDL, serum glucose, or blood pressure noted (subjects were normotensive).</td>
</tr>
<tr>
<td>Grünwald et al., 1992</td>
<td>Hypercholesterolemia (TC=6.5 mmol/L)</td>
<td>DB, MC n=184</td>
<td>18 weeks</td>
<td>200 mg, 3x/day</td>
<td>Subjects maintained a normal diet and medications</td>
<td>After garlic treatment and compared to baseline, mean serum TC decreased by 8% (p&lt;0.001); LDL decreased by a non-significant 5%; HDL increased by 5%; LDL: HDL improved by 12% (p&lt;0.05); TG levels decreased by a non-significant 11%. 23 patients with mild hypertension experienced a significant decrease of 7% in SBP (p&lt;0.05) and a non-significant 4% in DBP.</td>
</tr>
<tr>
<td>Holzgartner et al., 1992</td>
<td>Hyperlipoproteinemina (TC &gt;250 mg/ml) garlic vs. Bezafibrate</td>
<td>R, DB, MC, Cm n=198 (6-week pre-treatment with placebo and NCEP Step 1 diet)</td>
<td>12 weeks (NCEP Step 1 diet maintained throughout study)</td>
<td>900 mg/day or 600 mg Bezafibrate/day</td>
<td>Garlic powder preparations equivalent to Sapec®, Kwai® garlic powder</td>
<td>Compared to baseline, both medications caused a significant decrease in TC (26%) (p&lt;0.001), LDL (32%) (p&lt;0.001), and TG (30%) (p&lt;0.001) vs. placebo group (1%) reduction. HDL increased by 12% (p&lt;0.0001) vs. 4% for placebo (p&lt;0.05). No differences were observed between the two regimens.</td>
</tr>
<tr>
<td>Rotzsch et al., 1992</td>
<td>Alimentary hypercholesterolemia (after intake of fatty meals)</td>
<td>R, DB, PC n=24</td>
<td>6 weeks</td>
<td>300 mg/day or placebo and fatty meal</td>
<td>Sapec®, Kwai® garlic powder; fatty meal contained 100g butter</td>
<td>The postprandial increase of TG was reduced significantly in garlic group, and was up to 35% less compared to placebo. HDL-2 cholesterol tended to increase with garlic more than placebo.</td>
</tr>
<tr>
<td>Auer et al., 1990</td>
<td>Mild hypertension (DBP 95–104 mmHg; TC &gt;250, TG &gt;200)</td>
<td>R, DB, PC, C n=47 (garlic n=24; placebo n=23) (n=21 taking blood pressure medication)</td>
<td>12 weeks (after 7 week acclimation period)</td>
<td>200 mg/day or placebo</td>
<td>Kwai® garlic powder</td>
<td>Results indicated 13% decrease in DBP in garlic group vs. 4% for placebo (p&lt;0.01). SBP decreased by 17% in garlic compared with 5% in the placebo group (p&lt;0.05). Serum cholesterol and TG were significantly decreased after 8 and 12 weeks in garlic group vs. placebo (p&lt;0.05).</td>
</tr>
<tr>
<td>Mader et al., 1990</td>
<td>Hyperlipidemia (TC &gt;200 mg/dL)</td>
<td>R, DB, PC, PG, MC n=221 (garlic n=111; placebo n=110)</td>
<td>16 weeks</td>
<td>200 mg/day or placebo</td>
<td>Kwai® garlic powder</td>
<td>Experimental group experienced a 12% reduction in TC vs. a 3% reduction in placebo group (p&lt;0.001). TG decreased by 17% vs. 2% respectively (p&lt;0.001). The best effect was noted in patients with TC levels 251–300 mg/dL.</td>
</tr>
<tr>
<td>Vorberg et al., 1990</td>
<td>Hypercholesterolemia</td>
<td>R, DB, PC, PG n=40 (garlic n=20; placebo n=20)</td>
<td>16 weeks</td>
<td>300 mg, 3x/day</td>
<td>Sapec®, Kwai® garlic powder</td>
<td>Garlic group resulted in a significantly lower TC (p&lt;0.001), TG (p&lt;0.05), BP (p&lt;0.01), than placebo. A self-evaluation revealed a greater feeling of “well being” (p&lt;0.05).</td>
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### Cardiovascular (cont.)

Hyperlipidemia/Hypercholesterolemia/Hypertension/Related Risk Factors (cont.)

<table>
<thead>
<tr>
<th>Author/Year</th>
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<tbody>
<tr>
<td>Lau et al., 1987</td>
<td>Hypercholesterolaemia and hypertriglyceridae</td>
<td>DB, C, CC n=15</td>
<td>6 months</td>
<td>1 g/day</td>
<td>Kyolic® AGE capsules</td>
<td>Serum cholesterol level (220–440 mg/dl) significantly dropped (12–31%) with AGE compared to baseline. Serum LDL and triglycerides were also significantly reduced (p&lt;0.05) with AGE.</td>
</tr>
<tr>
<td>Bordia, 1981</td>
<td>Blood lipids in subjects with coronary heart disease</td>
<td>O (n=20) healthy volunteers or (n=62) patients with coronary heart disease</td>
<td>10 months</td>
<td>0.25 mg/kg of body weight/day or placebo</td>
<td>Garlic essential oil in gelatin capsules</td>
<td>Patients taking garlic experienced a decrease in serum cholesterol (p&lt;0.05) and LDL (p&lt;0.05), while an increase was observed in the HDL fraction (p&lt;0.05).</td>
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### Arterial and Fibrinolytic Activity

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<tr>
<td>Steiner and Li, 2001</td>
<td>Effects on platelet function</td>
<td>DB, CO, PC, R n=34</td>
<td>44 weeks (6-week baseline, 18-week supplementation, 18-week crossover; 2-week washout)</td>
<td>3 capsules (800 mg each) 3x/day</td>
<td>Kyolic® AGE capsules vs. placebo capsules</td>
<td>In placebo the atherosclerotic plaque (in carotid and femoral artery) increased by 15.6% over 4 years while decreasing 2.6% in experimental group (p&lt;0.001). Garlic diminished the age-related decrease in plaque volume by 6–13%. Atherosclerosis is reduced by high-resolution ultrasound. Results substantiate a preventive and curative role for garlic powder for atherosclerosis.</td>
</tr>
<tr>
<td>Koscielny et al., 1999</td>
<td>Arterial plaque (in patients with advanced atherosclerotic plaque)</td>
<td>R, DB, PC n=152</td>
<td>≥2 years</td>
<td>≥300 mg/day</td>
<td>Standardized garlic powder</td>
<td>Pressure-standardized elastic vascular resistance was lower in garlic groups than age-matched controls (p&lt;0.0001). Pulse wave velocity (PWV) correlated with age (r=0.44 garlic, r=0.52 control) and systolic blood pressure (SBP) (r=0.48 garlic group, r=0.54 control group) for both groups, but in garlic group an increase in age or SBP was associated with a smaller rise in PWV vs. controls. No difference noted in blood pressure, heart rate, and plasma lipid levels in both groups. Chronic garlic powder consumption attenuated age-related increase in aortic stiffness.</td>
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<tr>
<td>Breithaupt-Grogler, 1997</td>
<td>Age-related stiffening of the sorta (healthy adults)</td>
<td>E, CS, OB n=202</td>
<td>≥2 years</td>
<td>≥300 mg/day</td>
<td>Standardized garlic powder</td>
<td>A significant decrease (p&lt;0.01) in circulatory platelet aggregates (down 10.3%) and spontaneous platelet aggregates (down 56.3%) was observed in garlic group. Garlic group also decreased in DBP, plasma viscosity, and serum cholesterol.</td>
</tr>
<tr>
<td>Kiesewetter et al., 1993a</td>
<td>Platelet aggregation (juvenile ischemic attack)</td>
<td>DB, PC, PG n=60</td>
<td>4 weeks (following a 4-week washout period)</td>
<td>200 mg, 4x/day or placebo</td>
<td>Kwai® garlic powder</td>
<td>Observations in garlic group include spontaneous platelet aggregation disappearance, increase of 47.6% microcirculation of the skin, 3.2% decrease in plasma viscosity, mean DBP decrease from 74 to 67 (p&lt;0.05), and a drop in the mean fasting blood glucose concentration from 89.4 to 79.</td>
</tr>
<tr>
<td>Kiesewetter et al., 1991</td>
<td>Platelet aggregation</td>
<td>DB, PC n=120</td>
<td>4 weeks</td>
<td>400 mg, 2x/day or placebo</td>
<td>Garlic powder</td>
<td>Observations in garlic group include spontaneous platelet aggregation disappearance, increase of 47.6% microcirculation of the skin, 3.2% decrease in plasma viscosity, mean DBP decrease from 74 to 67 (p&lt;0.05), and a drop in the mean fasting blood glucose concentration from 89.4 to 79.</td>
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### Anticancer/Chemoprevention

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<tbody>
<tr>
<td>Dimitrov and Bennink, 1997</td>
<td>Effect on arachidonic acid metabolism</td>
<td>PS, O n=8 healthy female volunteers</td>
<td>3 months</td>
<td>10 mL extract/day mixed with orange or V8 juice in morning</td>
<td>Kyolic® aged garlic hydroalcoholic liquid extract</td>
<td>Compared to baseline, after 3 months of taking Kyolic® substantial decrease in serum PGE2 levels in majority of subjects. Results indicate that ethanol-water soluble extract is capable of modulating PGE2 and PGF2α.</td>
</tr>
<tr>
<td>Witte et al., 1996</td>
<td>Colon cancer</td>
<td>E, CC n=488</td>
<td>4 years</td>
<td>≥3 servings/week</td>
<td>Serving size unspecified</td>
<td>A reduction of 37% occurrence in pre-cancerous cells and colorectal polyps was observed. (Odds ratio = 0.63.)</td>
</tr>
<tr>
<td>Dimitrov and Gwilt, 1996</td>
<td>Effect on metabolism of acacetaminophen</td>
<td>O n=16 males (healthy, non-smoking)</td>
<td>3 months</td>
<td>10 mL extract/day mixed with 120 mL orange juice</td>
<td>Kyolic® aged garlic hydroalcoholic liquid extract plus acacetaminophen (500 mg Tylenol®)</td>
<td>Garlic treatment had no discernible effect on oxidative metabolism, but was associated with slight increase in sulfate conjugation of acacetaminophen. Study suggests that AGE has limited potential as a chemopreventive agent.</td>
</tr>
<tr>
<td>Steinmetz et al., 1994</td>
<td>Colon cancer</td>
<td>E, CH n=41,837</td>
<td>5 years</td>
<td>≥1 servings/week</td>
<td>Unspecified as to the quantity of a serving size</td>
<td>The study showed that risk of colon cancer in women ages 55–69 decreased with garlic consumption (rr=0.68).</td>
</tr>
<tr>
<td>You et al., 1989</td>
<td>Stomach cancer</td>
<td>E n=564 patients with stomach cancer; n=1,131 controls</td>
<td>15 years</td>
<td>0 kg/year; 0.1–1.5 kg/y; &gt;1.5 kg/y</td>
<td>Raw and cooked garlic</td>
<td>Significant trends were shown for the decrease of stomach cancer with garlic use. Odds ratio (95% CI) for highest compared with lowest garlic consumption was 0.7 (0.4–1.0, p=0.03).</td>
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### Other

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<tr>
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</tr>
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<tbody>
<tr>
<td>Rozenfeld et al., 2000</td>
<td>Bleeding potential of combined garlic and warfarin therapy</td>
<td>DB, PC, R n=8 patients (INR therapeutic for at least 2 months)</td>
<td>4 weeks</td>
<td>1,200 mg/day or placebo</td>
<td>Kyolic® AGE capsules</td>
<td>All patients took Coumadin®. No INR differences between groups noted (p&gt;0.05). Compared to baseline, no significant changes in INR values within each group (p&gt;0.05). No patients developed urine or stool bleeding. Kyolic® did not worsen side effects of Coumadin®.</td>
</tr>
<tr>
<td>Okuhara, 1994</td>
<td>Peripheral circulation</td>
<td>Cm, CO, R n=12 healthy male volunteers</td>
<td>5 months</td>
<td>1.6 ml GE or GEC/day or continuous administration test: 0.8 ml GE or GEC 2 x/day</td>
<td>Kyolic® aged garlic hydroalcoholic liquid extract plus heat-treated liquid preparation of garlic (GEC)</td>
<td>After single administration, skin temperatures in GE ( garage) group peaked at 60 minutes on backs of hands (p&lt;0.01) and 90 minutes on backs of feet (p&lt;0.01). In GEC (control) group, peaked at 30 minutes on backs of hands and feet. After 14 days continuous use, higher skin temperatures in GE group on backs of hands and feet and on only backs of feet in GEC group. Study suggests improved blood flow with GE.</td>
</tr>
<tr>
<td>Kiesewetter et al., 1993b</td>
<td>Intermittent claudication (Peripheral Arterial Occlusive Disease Stage II)</td>
<td>DB, PC n=80</td>
<td>12 weeks</td>
<td>200 mg, 4x/day or placebo</td>
<td>Kwai® garlic powder</td>
<td>A significant increase (p&lt;0.05) was observed in walking distance by the 5th week and correlated to a simultaneous decrease in spontaneous platelet aggregation in garlic group vs. placebo. Garlic group also had decrease in diastolic blood pressure (DBP), plasma viscosity, and serum cholesterol.</td>
</tr>
<tr>
<td>Abdullah et al., 1989</td>
<td>Effects on natural killer (NK) cell activity in HIV+ patients</td>
<td>PS n=7</td>
<td>12 weeks</td>
<td>5 g/day 1st 6 weeks; 10 g/day 2nd 6 weeks</td>
<td>Aged processed garlic preparation: Special Garlic Preparation (SGP)</td>
<td>After 6 weeks, 6 of 7 qualified patients had normal NK activity, and all had normal NK activity at 12 weeks. Helper/suppressor ratio improved in 4 of 7 patients. Conditions of diarrhea, genital herpes, candidiasis and pansinusitis with recurrent fever also improved during the study.</td>
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