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Historical, Chemical and Cardiovascular Perspectives on Garlic: A Review

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ABSTRACT

The objective of this review is to highlight the historical background, constituents, chemistry and use of Garlic in Cardiovascular Disease. Garlic (*Allium sativum*) has been used medicinally since antiquity. In virtually every early civilization known, such as ancient India, Egypt, Rome, China, and Japan, garlic was part of the therapeutic regimen for a variety of maladies. Therefore, the ancient medicinal tradition of garlic use would qualify it as a folk medicine or as an alternative or complementary medicine. Many derivatives of dithiines, allyl sulfides, and ajoenes are in use or being evaluated for use.

KEYWORDS: Garlic, dithiines, allyl sulfides, and ajoenes.

INTRODUCTION

The word *garlic* comes from Old English *garleac,* meaning *"spear leek."* Garlic (*Allium sativum*) is a bulbous root with a strong taste and smell. Garlic is believed to have originated in Central Asia and belongs to the Alliacae family. It is used widely in culinary preparations and as a folk medicine.

CHEMISTRY OF GARLIC

The majority of garlic (65%) is water, and the bulk of the dry weight is composed of fructose-containing carbohydrates, followed by sulfur compounds, protein, fiber, and free amino acids (1). It also contains high levels of saponins, phosphorus, potassium, sulfur, zinc, moderate levels of selenium and Vitamins A and C, and low levels of calcium, magnesium, sodium, iron, manganese, and B-complex vitamins; garlic also has a high phenolic content (2). A majority of the compounds present in garlic are water-soluble (97%) with small amounts of oil-soluble compounds also present (0.15–0.7%) [Table. 1].(give a list of these in a tabular format). Intact garlic bulbs contain a high amount of γ-glutamylcysteine.

Theodor Wertheim, a German chemist was the first to carry out a chemical study of garlic (3-4). In 1844 he extracted 'garlic oil' from garlic by steam distillation. He commented on the sulfurous nature of this oil, and named the hydrocarbon group present 'allyl'. This name is still in use today, it describes the group CH_2=CH-CH_2-. Semmler in 1892 identified a component of the oil as diallyl disulfide.

Cavallito discovered an unstable, odoriferous liquid substance in extracts of fresh garlic. He termed allicin (CH_2=$CHCH_2S(O)SCH_2CH$=CH_2≡AllS(O)SAll, 2-propene- 1-sulfinothioic acid S-2-propenyl ester; 2) which in turn are produced by the action of the enzyme alliinase on cysteine derivatives. Garlic alliinase was first described in 1947 (5). It is a homodimeric enzyme of 2 × 448 amino acid residues and a total molecular weight of 103,000. The enzyme contains one pyridoxal-5'-phosphate (PLP) cofactor per subunit and belongs to the class I of PLP-dependent enzymes (6). Stoll and Seeback identified the immediate precursor of allicin as alliin, CH_2=$CHCH_2S(O)CH_2CH(NH_2)COOH$,(+)-S-allyl-L-cysteine S-oxide; 3).

The biochemical reactions that occur in chopped garlic were first probed in 1948 by Stoll and Seebeck of the Sandoz chemical company. They explained why the formation of allicin occurs only on cutting by an enzyme catalyzed mechanism (Fig. 1). When garlic is chopped or crushed, the garlic tissue is damaged and the precursor, alliin comes into contact with the enzyme allinase. It was later discovered that another biological compound, pyridoxal phosphate, must also be present. The enzyme catalyses the decay of alliin to an unstable intermediate, 2-propenesulfenic acid. This dimerizes to give allicin. Allicin is also unstable and reacts with other compounds present to give many products (3-4).

Now it is clear that most of them rely on sulfur-containing garlic components. Many of the active compounds have been identified in garlic and other *Allium* species and found to belong to one of three groups: dithiines, allyl sulfides, and ajoenes. Their organic chemistry has been studied (7) and in some cases their therapeutic effects have been elucidated (8).

HISTORY OF GARLIC

Ancient Egypt: As listed in Table 2, the earliest known references indicate that garlic formed part of the daily diet of many Egyptians. It was fed particularly to the working class involved in heavy labour, as in the building of the pyramids (9). Indeed, a recurring theme throughout early history is that garlic was given to the labouring classes, presumably to maintain and increase their strength, thereby enabling them to work harder and be more productive. Whether garlic was also consumed with the same diligence

by the upper classes is less certain. It is of interest in this connection that when King Tutankhamen's tomb, which dates from; 1500 BC, was excavated in 1922, cloves of garlic were clearly identified (10, 11). What purpose did the garlic serve in the tomb? Did it have religious significance? Was it a

reminder of daily life of Egypt, or was it left by a careless workman during a lunch break? We do not know the answers to these questions, but the presence of garlic in the tomb is strong evidence that the vegetable was in use at the time. The authoritative medical text of the era was the *Codex Ebers* a 3,500 years old document (12, 13), which consisted of a number of volumes. Several of the treatments authorized the use of garlic. The *Codex Ebers* is one of the earliest sources indicating prescription of garlic for the treatment of abnormal growths. It is probable that these growths represented malignancies of one kind or another. Abscesses would also have fit into this category. The *Codex* also prescribed garlic for circulatory ailments, general malaise and infestations with insects and parasites.

Biblical: According to the *Bible*, the Jewish slaves in Egypt were fed garlic and other allium vegetables, apparently to give them strength and increase their productivity, as it was believed to do for the indigenous Egyptian citizens. The Jewish people must have developed some fondness for garlic, because when they left from Egypt with Moses, it is written (Table 3) that they missed "the fish. The cucumbers, and the melons, and the leeks, and the onions and the garlic" (12, 14). It is unlikely that garlic had religious significance for the Jews, although this possibility cannot be excluded. The Talmud, a Jewish religious text dating from the 2nd century AD, prescribes patterns of behaviour, including the consumption of garlic for the treatment of infection with parasites and other disorders (9). Although in contemporary life one does not tend to ascribe romantic properties to garlic, its use was recommended by the Talmud to promote relations among married couples, perhaps as an aid to procreation.

Ancient Greece: As noted in Table 4, excavations of ancient Greek temples have unearthed garlic, and the palace of Knossos in Crete, dating to; 1400–1800 BC, containedwell-preserved garlic when it was excavated (9). As with the Egyptians, garlic was associated with strength and work capacity. Garlic formed an important part of the military diet, particularly when soldiers were off to battle. There is evidence that during the earliest Olympics, which originated in Greece, garlic was fed to the athletes before they competed (10, 13), conceivably functioning as one of the first of the so-called "performance enhancing" agents used in competitive athletics. If so, one wonders whether there were prescribed doses, clinical trials and limits placed on the amounts consumed. One imagines that there must have been someone in authority supervising the activities of the athletes as they prepared themselves for the sports competition. Hippocrates, widely regarded as the father of Medicine, made garlic a part of his therapeutic armamentarium, advocating its use for pulmonary complaints, as a cleansing or purgative agent, and for abdominal growths, particularly uterine (9). As in the cultures discussed above, garlic appears to have been consumed primarily by the lower classes. It appears not to have been a favourite food item among the ruling classes and its presence in religious temples was not permitted (9), a proscription also found in certain Asian cultures.

Ancient Rome: As in Greece, the Romans perceived garlic as an aid to strength and endurance; it was fed to both soldiers and sailors (10) and was part of a ship's manifest when it set out to sea. With the emergence of Rome as a leading power, Greek medicine and its traditions gradually were transferred to Rome. The leading medical authority was the Greek, Dioscorides (12, 15), who served as the chief physician for Nero's army (Table 5). He was the author of a five-volume treatise that recommended garlic because it "cleans the arteries." It should be noted that the circulation of the blood was not discovered until hundreds of years later, and contemporary beliefs held that arteries transported air throughout the body, whereas veins were known to transport blood. Clearly, the concept that cardiovascular status may be improved by garlic, presently a subject of active research, has origins in antiquity. Garlic was also recommended for disorders of the gastrointestinal tract, for treatment of animal bites and for alleviation of joint disease and seizures. Medicine in Rome was greatly influenced by the writings of Pliny the Elder, a Greek physician who wrote the five-volume *Historica Naturalis* (9, 12). Twenty three uses for garlic were listed for a variety of disorders. Among these was that garlic was believed to confer significant protection against toxins and infections, a finding corroborated by contemporary investigations of the effects of garlic upon activities of P450-2E1 and other hepatic degradative diseases (16, 17).

Ancient China and Japan: The use of garlic as a food and as a medicinal agent has ancient origins in Asia. The best estimate is that by or before 2000 BC, garlic was in wide use in China and formed part of the daily diet, particularly when consumed together with raw meat (9, 11). Records dating from that era suggest that garlic was also used as a food preservative, as listed in Table 6. In ancient Chinese medicine, garlic was prescribed to aid respiration and digestion, most importantly diarrhoea and worm infestation (18). As a spicy food, its regular consumption was recommended but in limited quantities. Evidence also suggests that garlic was utilized to treat sadness or depression as well. Chinese medicine has historically been associated with the use of combinations of herbs to form a healing tonic, rather than the administration of single agents. Allium was evidently frequently used in combination therapy. Fatigue, headache and insomnia were often treated with garlic. There are also indications that garlic was used to treat and improve male potency (11). It is believed that garlic was introduced in Japan later than in China, probably; 2000 years ago (11).

Ancient India: Garlic has been associated with the healing process in India from the time of the first available written records. Three ancient medical traditions, i.e., Tibbi, Unani and Auryvedic, made extensive use of garlic as a central part of the healing efficacy of plants (9). The leading surviving medical text, *Charaka-Samhita*, recommends garlic for the treatment of heart disease and arthritis 2000 years ago as listed in Table 7 (18). A later manuscript, dating to; 300 AD, advanced the use of garlic for infections, infestations and worms, weakness and fatigue, and a variety of digestive disturbances. This text, nearly as old as the *Charaka-Samhita*, is known as the Bower manuscript because, after being found

in an ancient tomb, it was purchased by a British Army officer, Hamilton Bower, late in the 19th century, who then made it available to scholars. Garlic was also observed to have a diuretic effect. It is possible that the mobilization of fluid from the extra-vascular space may have been due to improved cardiovascular function resulting from garlic treatment. Some religious sects did not permit the consumption of garlic or onions, rather as the Greeks and Romans proscribed garlic in the temples (9). Garlic either was not permitted or fancied by the upper Brahmin classes, whereas in other castes, it was applied externally to help repair cuts, bruises and infections, and it comprised one of a number of perceived aphrodisiacs available from natural plant sources (11).

Middle Ages: Garlic became available in Europe after the Roman legions moved north. During Medieval times, knowledge of the therapeutic use of plants, particularly garlic, was gained and transmitted through the monks. Garlic was grown in the monasteries. The leading text of the middle ages was the *Hortulus* manuscript from shortly after 800 AD, as noted in Table 8 (9). This volume described all of the plants growing in one cloister that were thought to have medicinal properties: Garlic featured prominently; it is interesting in that there does not seem to have been any objection to its use in a religious setting in that era, in contrast to its rejection by religious leaders in earlier cultures. Garlic was believed to alleviate constipation when consumed with beverages. Workers outdoors were advised to consume garlic to prevent heat stroke (9, 11). The recommendation of garlic for those who had to do hard physical labour is a recurring theme dating to antiquity. Another recurring theme is of the upper classes tending to reject garlic and not consider it fit for their consumption. A leading physician during the latter part of the 12th century, the Abbess of Rupertsberg, St. Hildegard von Bingen (11, 13), gave garlic a prominent role in her medical writing. Curiously, she came to the conclusion that raw garlic was more effective than cooked garlic, perhaps because the latter has less pungency then the former. In the Medical School at Salerno, one of the most influential centers of medical learning at the time, food played an important role in the treatment of disease as well as in the preservation of good health. Garlic was classified as a "hot food" to be consumed during the winter to limit the development of pulmonary or breathing disorders (9). Garlic was also utilized against massive debilitation and later in the Great Plagues (12, 18).

The Renaissance: With the onset of the Renaissance, increasing attention was paid in Europe to the medical uses of plants. So-called "physic" gardens were established at leading universities to grow plants of medicinal value. Garlic was one of the major plants grown for this purpose (Table 9). A leading physician of the 16th Century, Pietro Mattioli of Siena, wrote widely, and his work was translated into several other languages. He prescribed garlic for digestive disorders, infestations with worms and renal disorders, as well as to help mothers during difficult childbirth (9). There are indications that during this time, many of the ruling classes in Continental Europe began to adopt garlic and not restrict its consumption to the working classes. It is said that King Henry IV of France in the late 16th and early 17th centuries was baptized in water containing garlic to protect him from evil spirits and probably from disease. In England, however, garlic remained the food of the working classes, a view that did not prevent the wealthier English from enjoying the therapeutic properties of garlic, i.e., it was recommended for constipation, toothache, dropsy, animal bites and the plague. Its purported beneficial effects in treating dropsy suggest that it was thought to improve cardiovascular function, mechanisms of which are only now under study. Doctors carried cloves of garlic with them at all times to protect themselves from the odour of disease (9).

Early America: Moving closer to contemporary times, it is worth recalling that bulbs similar to garlic grew freely in the woods of North America and that Native Americans used garlic in their tea (Table 10). It was brought to the new world by the explorers and sailors from France and Portugal. Later in the 19th century, garlic formed an important part of the Shaker medical armamentarium as a stimulant, expectorant and tonic. Garlic's perceived therapeutic properties were all accepted by large groups of the population (9). The *Home Book of Health*, authored by John Gunn in 1878, featured garlic prominently; it was recommended as a diuretic, for treatment of infections, as a general tonic and for asthma and other pulmonary disorders (9). In the early part of the 20th century, in the volume *Health Remedies, a Complete Medical Work and Family Guide*, garlic was promoted for diseases of the lung in children and adults.

CARDIOVASCULAR EFFECTS OF GARLIC

In vitro (preclinical) studies

Numerous in vitro studies have confirmed the ability of garlic to reduce parameters associated with cardiovascular disease. A brief description of some of these studies is given below.

Cholesterol and lipid-lowering effects: Several studies have indicated that garlic and its constituents inhibit key enzymes involved in cholesterol and fatty acid synthesis in cultured rat hepatocytes and human HepG2 cells (19-22). Direct measurements of enzyme activity have indicated that garlic and various constituents inhibit human squalene monooxygenase and HMG-CoA reductase, enzymes involved in cholesterol biosynthesis (19,23). This inhibition of HMG-CoA reductase by garlic has also been confirmed in a recent study (24). It has also been shown that the more water-soluble compounds like S-allylcysteine (SAC) present in aged garlic extract are less cytotoxic and more efficient in inhibiting cholesterol biosynthesis than the lipid-soluble sulfur compounds such as diallyl sulfide (DAS) (21).

Antithrombotic and anti-platelet aggregatory effects: Platelet aggregation and subsequent thrombus formation are significantly reduced by garlic and its constituents. Chloroform/acetone extracts of fresh garlic have been shown to inhibit cyclooxygenase activity directly in cell-free assays, with the acetone extract being more effective (25). In this study, the chloroform extract of garlic was a more effective inhibitor of ADP- and platelet-activating factor (PAF)-induced platelet aggregation. The mechanism of inhibition of platelet aggregation by garlic's constituents has also been addressed,

Table 1: Water soluble and oil soluble compounds in Garlics.

Water-soluble	Oil Soluble
S-allylcysteine	Diallyl disulphide
Alliin	Diallyl trisulphide
S-propylcysteine	Methylallyl sulphide
S-ethylcysteine	Dipropyl disulphide
S-methylcysteine	Dipropyl sulphide
Se-(methyl) selenocysteine	Allyl mercaptan
Selenomethionine	Allyl methy sulphide
Selenocystine	

Table 2: Ancient Egypt

Garlic as part of the daily diet
Medical text *Codex Ebers* gives remedies based on the use of garlic
Well-preserved garlic cloves were found in the tomb of King Tutankhamen

Table 3: Biblical

Garlic as part of the daily diet
On leaving Egypt, slaves missed their "fish, cucumbers, melons, leeks, onions and garlic"
Talmud recorded many benefits of garlic, and recommended it for married couples

Table 4: Ancient Greece

Garlic found in the palace of Knossos in Crete
Soldiers were fed garlic to give them courage, and garlic was associated with war
During the first Olympic games, garlic was taken by athletes before they competed
Used to protect the skin against poisons or toxins
Hippocrates, the Father of Medicine, used garlic

Table5: Ancient Rome

Garlic was fed to troops and to sailors for strength
In *Historica Naturalis* garlic was prescribed for digestion, animal bites, arthritis and convulsions
Later garlic was used for respiratory ailments and for parasites

Table 6: Ancient China and Japan

Garlic used as a food preservative
Formed part of the daily diet with raw meat
Prescribed as aid to digestion and respiration, to provide energy and lift depression
May have been used to improve male potency

Table 7: Ancient India

In medical text Charaka-Samhita, garlic was used to treat heart disease and arthritis
In another ancient medical text, known as the Bower manuscript (named after its discoverer), garlic was used for fatigue, parasites, digestive diseases and leprosy

Table 8: Middle Ages

Christian monks preserved knowledge of benefits of plants, including garlic
The *Hortulus* manuscript described use of garlic
Garlic recommended raw rather than cooked by the Abbess of Rupertsberg
The medical school of Salerno taught dietetics utilizing garlic prominently
Garlic used as a treatment for the Great Plagues

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Table 9: The Renaissance

"Physic" gardens were opened in Padua, Pisa, Zurich, Bologna and other cities
Dr. Pietro Mattioli of Siena advised garlic for digestive disorders, kidney stones and expelling afterbirth
Henry IV of France baptized in water containing garlic
The English included garlic in their medicine chests, and it was used for toothache, constipation, dropsy and plague

Table 10: Early America

Native Americans used garlic in a tea to treat flu-like symptoms
Garlic was used in Shaker herb catalogs as a Stimulant, expectorant and tonic (1825)
Dr. John Gunn used garlic in the Home-Book of Health as a diuretic, expectorant and treatment for worms (1878)
Dr. Joseph Richardson, author of Health Remedies, used garlic for all lung diseases.

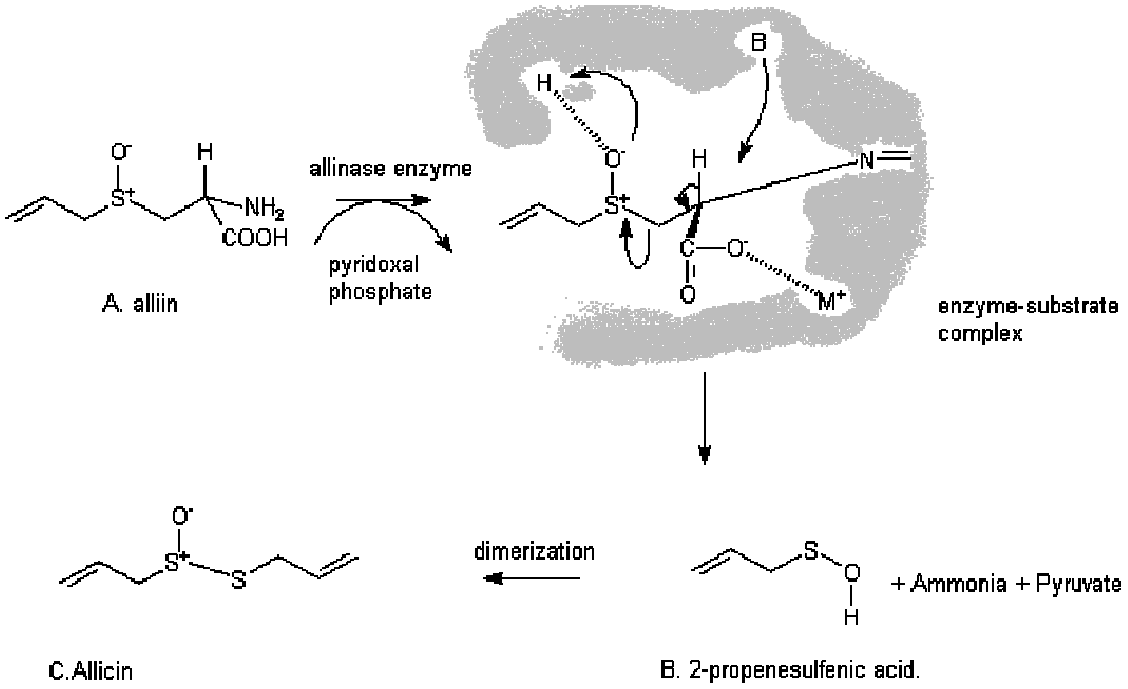

Fig. 1: Pathway for the formation of allicin from alliin

and it is thought to work via the inhibition of calcium mobilization (26). Ajone, another garlic derivative, has also been shown to inhibit platelet aggregation in vitro (27). A recent study has also found another garlic component, sodium 2-propenyl thiosulfate, to modulate cyclooxygenase activity in canine platelets, thus preventing their aggregation (28).

Blood coagulation, fibrinolysis and circulatory effects: Fibrinolysis is also enhanced by garlic, resulting in dissolution of clots and thrombi. In vitro studies have demonstrated that aged garlic extract improves circulation and blood properties by preventing lipid peroxidation and hemolysis in oxidized erythrocytes (29). A recent study has confirmed that garlic improves the fluidity of erythrocytes isolated from hypercholesterolemic rats (30). In contrast, garlic oil extracts and the allyl sulfides were unable to protect isolated erythrocytes from t-butyl hydroperoxide-induced hemolysis (31). Blood pressure and vascular tone effects. A garlic extract has been shown to modulate the production and function of both endothelium-derived relaxing factor (NO) and constricting factors (endothelin-1) in isolated rat pulmonary arteries (32). Garlic juice has also been shown to have some beneficial effect on heart rate; however, at higher dosages it exerts undesirable effects (33). gamma-Glutamylcysteines are compounds found in garlic, and these may lower blood pressure, as indicated by their ability to inhibit angiotensin-converting enzyme *in vitro* (34).

Effects on endogenous antioxidant defences: Numerous studies have investigated the antioxidant properties of garlic in various in vitro systems; some of these are outlined below. Garlic has been shown to inhibit the in vitro oxidation of isolated human LDL by scavenging superoxide (ROS) and inhibiting the formation of lipid peroxides (34, 35). In vitro studies have shown that AGE prevents the depletion of intracellular glutathione (GSH) when endothelial cells are

incubated with oxidized LDL (36). AGE also increases GSH levels in vascular endothelial cells by modulation of the GSH redox cycle and increases glutathione disulfide (GSSG) reductase activity while increasing SOD activity (37). *In vitro* (preclinical) studies have confirmed that garlic has the ability to reduce parameters associated with cardiovascular disease. However, such studies need to be translated into a clinical setting, the results of which are discussed below.

***In vivo* (clinical) studies**

A limited number of clinical trials have been conducted with different garlic preparations. In this review an attempt has been made to critically review human trials, which have been conducted since 1993. Only those trials that were conducted for a minimum period of 2 wk and that addressed the following parameters have been included: (a) cholesterol-lowering effects, (b) inhibition of platelet aggregation, (c) lowering of blood pressure, and (d) other cardioprotective properties.

Cholesterol-lowering effects: Since 1993, 25 clinical trials have been published that have investigated the hypolipidemic effects of garlic (38-45). Fourteen of the studies showed that garlic had no effect on lowering cholesterol, but 11 studies showed a reduction in serum cholesterol. It is interesting to note that of the 14 studies showing no effects, 5 were in normolipidemic subjects, 8 were in moderately hypercholesterolemic subjects, and 1 study was in teenagers with familial hypercholesterolemia. A further breakdown of these 14 studies shows that 9 used garlic powder, 4 used AGE, and 1 used steam-distilled garlic oil. The 11 studies that showed a positive effect on cholesterol reduction were performed in hypercholesterolemic subjects; 5 studies used AGE, and the rest used garlic powder. It is apparent that garlic is effective in hypercholesterolemic subjects, and it may well be that a reduction in cholesterol will be seen only above a certain threshold. Another factor that may need to be taken into account is the gender of the subjects. Zhang et al. (41) reported that gender might affect the action of garlic on plasma cholesterol and glucose levels of normal subjects. A systematic review of the effectiveness of garlic as an antihyperlipidemic agent was published in 2003 by Alder et al. (46). They included 10 studies and found that in 6 studies garlic was effective in reducing serum cholesterol levels. The average drop in total cholesterol was 9.9%, LDL 11.4%, and triglycerides 9.9%. Earlier meta-analysis has also confirmed that garlic is superior to a placebo in reducing total cholesterol levels (47, 48). However, the size of the effect is modest, and the robustness of the effect is open to question.

Inhibition of platelet aggregation: Since 1993, 7 clinical trials have been performed, and all have shown that garlic consumption leads to the inhibition of platelet aggregation (61, 38, 49). Of these 7 studies, 4 were performed in healthy subjects, and 3 in subjects with coronary artery disease/mild hypercholesterolemia. Two studies involved garlic powder, 1 oil extract, 1 ethyl acetate extract, and 3 studies involved aged garlic extract. Garlic has a positive response in the inhibition of platelet aggregation in both healthy subjects and subjects with cardiovascular disease.

Lowering of blood pressure: Since 1993, 9 studies have been published on the effects of garlic on blood pressure (38,45, 50,51). Two studies used AGE, 3 used garlic powder, and 1 used garlic in the diet, and all these studies showed a reduction in blood pressure. Three studies utilized Kwai garlic and did not report any change in the blood pressure. In support of this, a meta-analysis published in 2001 (48) concluded that garlic has insignificant effects on blood pressure.

Other cardioprotective properties: Oxidative stress can lead to the pathogenesis of cardiovascular disease, and some clinical trials involving garlic have addressed this. Seven studies since 1993 have been identified. One was performed in patients with essential hypertension, and garlic pears were used. A reduction in blood pressure and a decrease in oxidative stress were reported (50). Four studies (2 in normal subjects, 2 in hypercholetrolemic subjects) used AGE and reported a decrease in oxidative stress (51-54). In contrast, 2 studies utilizing garlic tablets (1 in normal subjects and 1 in hypercholeterolemic subjects) did not show a reduction in oxidative-stress parameters (38,55). One of the studies, which showed a reduction in oxidative stress after garlic ingestion, was conducted in our laboratory in healthy smoking and non-smoking men and women (53). In this study F2-isoprostanes were measured because their quantification in plasma and urine is a sensitive and specific indicator of oxidative stress *in vivo*. Dietary supplementation with AGE for 14 d reduced plasma and urine concentrations of F2-isoprostanes by 29% and 37%, respectively, in non-smokers and by 35% and 48%, respectively, in smokers. Fourteen days after cessation of dietary supplementation, plasma and urine concentrations of F2-isoprostanes in both groups returned to values not different from those before ingestion. It was also observed in this study that the plasma antioxidant capacity of non-smokers was approximately twice that of smokers. Interestingly, the plasma antioxidant capacity of smokers significantly increased by 53% following supplementation with AGE for 14 d. However, after the 2-wk washout period (day 28), the plasma antioxidant capacity of smokers decreased by 49% and was now similar to that before AGE ingestion; the plasma antioxidant capacity of non-smokers
remained unaffected during this same period (53). The subjects in this study were normolipidemic, and no other changes including those of serum lipids were seen in this study. This underscores the point that multiple questions must be addressed in clinical trials incorporating any new and specific markers. The conclusion from this study was that dietary supplementation with AGE reduces oxidative stress in humans and thus may prevent or delay chronic diseases such as cardiovascular disease. Other direct cardioprotective effects of garlic in humans have also been reported, such as a decrease in unstable angina (56), an increase in the elastic property of blood vessels (57), and a decrease in peripheral arterial occlusive disease (58). More recently, garlic has been shown to increase peripheral blood flow in healthy subjects (59) while inhibiting the progression of coronary calcification in patients receiving statin therapy (60). However, the number of trials conducted within this area is limited.

CONCLUSION

In this cursory overview of garlic in early history, several issues emerge as recurring themes. We have much to learn from the ancients as we adopt a historical perspective and seek to elucidate the mechanisms of action of garlic and its derivatives and to establish its ultimate role in the prevention and treatment of disease. In short, evidence from clinical trials points toward garlic having a role to play in either preventing or delaying cardiovascular disease. However, further research is required to convince health workers, consumers, and regulatory bodies.

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