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PHARMACOLOGICAL PROPERTIES OF GARLIC: A REVIEW

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ABSTRACT

Garlic has been used medicinally since antiquity. Almost in 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. In many cultures, garlic was administered to provide strength and increase work capacity for laborers. Hippocrates, the revered physician, prescribed garlic for a variety of conditions. Garlic was given to the original Olympic athletes in Greece, as perhaps one of the earliest performance enhancing agents. It is of interest that cultures that developed without contact with one another came to similar conclusions about the efficacy of garlic. Louis Pasteur studied the antibacterial action of garlic in 1858. in the first world war, garlic was widely used as a antiseptic to prevent gangrene and today people use garlic to help prevent atherosclerosis and improve high blood pressure. Modern science is tending to confirm many of the beliefs of ancient cultures regarding garlic, defining mechanisms of action and exploring garlic's potential for disease prevention and treatment.

INTRODUCTION

The word *'Allium sativum'* is derived from two sources, the Celtic word *allium,* meaning "hot or burning," and the Latin second name *sativum* meaning "cultivated." Our familiar word *garlic* is from the Anglo-Saxon word *garleac,* a combination of *gar* meaning spear and lac that means leek. Garlic is the best example of a medicinal food. It is one of the most intensively studied herbs in natural medicine today.Garlic contains hundreds of constituents, with at lest 23 sulphur compounds having been identified. The strong smelling juice of the bulbs contains a mixture of aliphatic mono and polysuiphides. Garlic is a minor source of selenium, chromium, potassium, germanium, calcium, iron, and vitamins A, C and B complex[1]. The major constituents of garlic are,

Allium

CAS Registry number: [556-27-4]

CAS name(s) : (S)-3-(2-Propenylsulfinyl)- L.-alanine; 3-((S)-allylsulfinyl)-L-alanine .

Molecular formula : $C_5H_{11}N0_3S$

Molecular weight : 17.22

Percent Composition.: C 40.66%, H 6.26%, N 7.90%, O 27.08%, S 18.09%

Allicin

CAS Registry number: [539-86-6]

CAS name(s): 2-Propene-1-sulfinothioic acid 5- 2-pro penyl ester

Molecular formula: $C_6H_{10}0S_2$

Molecular Weight: 162.28.

Percent Composition: C 44.41%, H 6.21%, 0

9.86%, S 39.52%.

Ajoene

CAS Registry number: [92285-01-3]

CAS name(s) : 2-Propenyl 3-(2- propenylsulfinyl)-1 -propenyl disulfide;

Molecular formula : $C_9H_{14}0S_3$

Molecular weight : 234.41.

Percent Composition: C 46.12%, H 6.02%, O 6.83%, S 41.04%.

TRADITIONAL MEDICINAL USES

Among practitioners of Ayurvedic medicine, garlic is held in high regard as an aphrodisiac and for its ability to increase semen. Fresh bulb juice is taken orally as an abortifacient. Two to three tablespoons of extract causes abortion within 12 hours. Twenty grams of the paste is given on the third day of menstruation [2]. Hot water extract of bulb is taken orally as an emmenagogue[3]. and anthelmintic[4]. For leukorrhagia, garlic bulb is mixed with leaves of Ziziphus mauritiana, pepper, and salt and taken with buttermilk. [5]. Hot water extract of dried bulb, mixed with an equal amount of honey is taken once a day for three days for whooping cough. [6]. Hot water extract of dried seeds is taken orally as an emmenagogue [7]. Infusion of the entire plant along with sugar is drunk to treat fever [5]. A patient with a second-degree burn of the forehead, induced by topical application of crushed garlic is also reported. Other folk medicine cultures have traditionally used garlic for treating colds and flu, fever, coughs, headache, hemorrhoids asthma, arteriosclerosis, low blood pressure, both hypoglycemia and hyperglycemia, cancer and as an aphrodisiac.

The epidemiological, clinical and laboratory data have shown that garlic contains many biologically active compounds which are beneficial to human health in general. Among all, one garlic- preparation called aged garlic extract is proven to be safer. Although additional studies are warranted in humans, compelling evidence supports the health effects attributed to aged garlic extract and its implications in preventing or reducing the risk of cardiovascular ailments, stroke and cancer.

Aizheimer's disease

Recently, the beneficial effects of garlic and its constituents on neuronal physiology and brain functions are beginning to emerge. However, this field is still in infancy and not yet fully explored: This encompasses multiple health effects of garlic and its constituents with reference to neuroprotection. Possible potential of dietary garlic as an alternative herbal pharmacotherapy for Alzheimer's disease is discussed.[8]

Antibacterial activity

Louis Pasteur was the first to describe the antibacterial effect of onion and garlic juices. Historically, garlic has been used worldwide to fight bacterial infections. Allium vegetables, particularly garlic exhibit a broad antibiotic spectrum against both gram-positive and gram-

negative bacteria. Noteworthy results published include the following: 1) raw juice of garlic was found to be effective against many common pathogenic bacteria-intestinal bacteria, which are responsible for diarrhea in humans and animals; 2) garlic is effective even against those strains that have become resistant to antibiotics; 3) the combination of garlic with antibiotics leads to partial or total synergism; 4) complete lack of resistance has been observed repeatedly; 5) even toxin production by microorganisms is prevented by garlic [9]. Ethanol (95%) extract was active on Escherichia coil, Salmonella typhosa, Shigelia sonnei, and Staphylococcus aureus [10]. Butanol, water and hot water extracts of fresh bulb on agar plate, at variable concentration was active on Bacillus subtilis H-17(Rec+), M-45(Rec-).[11]. Decoction of dried bulb on agar plate was active on Pseudomonas aeruginosa. Hot water extract at a concentration of 62.5 mg/ml was active on Staphylococcus aureus and inactive on Escherichia coIl. [12].Fresh essential oil, undiluted on agar plate, was active on Pseudomonas aeruginosa and Staphylococcus aureus, and inactive on Bacillus cereus and E. coli. [13]. Leaf essential oil on agar plate was inactive on Bacillus cereus, E. coli Pseudomonas aeruginosa, and Staphylococcus aureus[14].Tincture of dried bulb on agar plate, at a concentration of 30.0 µl/disk (10 gm plant material in 100 ml ethanol) was active on *Escherichia coli*, Pseudomonas aeruginosa, and Staphylococcus aureus. [15].

The antibacterial activity of the crude aqueous extract of garlic was investigated against some pneumonia causing bacteria by an agar dilution technique. The results revealed that Streptococcus pneumoniae standard test organism was completely inhibited by 7.8 mg/ml of media and the clinical isolate of Klebsiella pneumoniae was completely inhibited by 24.38 mg/ml of media, indicating that Streptococcus pneumonia is the most sensitive and Klebsiella pneumoniae the least. Garlic could be used as an effective antibacterial agent for this pathogenic microorganisms. [16].

Anti carcinogenic effects

Garlic treatment resulted in a fraction of cells detaching from the culture flasks. These cells remained viable. Flow cell cytometry showed that untreated cells exhibited a normal distribution among phases of the cell cycle, with 12% of cells at the G2 / M boundary. Of the garlic-treated cells remaining attached to the flask, 27% were present at the G2/M boundary. Treated cells that detached from the flask were found almost exclusively (89%) at the G2/M boundary. RNA fingerprinting and microarray analysis showed that expression of the gene for menin was twice

as high in control celIs as in detached treated cells. In contrast, expression of genes for epidermal growth factor receptor and integrin-alpha6 was nearly twice as high in detached treated cells as in control cells. ,These changes in gene expression were consistent with an arrest of the cell cycle at the nG2/M boundary. Garlic's arrest of the cell cycle in human adenocarcinonia cells may explain in part its anticarcinogenic properties [17].

The novel anticarcinogenic activity of diallyl disulfide, a naturally occurring organosulfidé from garlic. Oral administration of diallyl disulfide resulted in a dose-dependent and significant inhibition of the growth of H-ras oncogene transformed NIH 3T3 cells implanted in nude mice. The results indicate that diallyl disulfide inhibits the growth of H-ras oncogene transformed tumors in vivo by inhibiting the membrane association of p21(H-ras) and that the allyl group is an important determinant in the inhibitory effect of this organosulfide on tumor growth[18]. Epidemiological and laboratory studies provide insight into the anticarcinogenic potential of garlic and its constituent compounds. Both water- and lipid-soluble allyl sulfur compounds are effective in blocking a myriad of chemically induced tumors. Part of the protection from these compounds probably relates to a block in nitrosamine formation and metabolism. However, blockage in the initiation and promotion phases of the carcinogenicity of various compounds, including polycyclic hydrocarbons, provide evidence that garlic and its constituents can alter several phase I and II enzymes. Their ability to block experimentally induced tumors in a variety of sites including skin, mammary and colon, suggests a general mechanism of action. Changes in DNA repair and in immunocompetence may also account for some of this protection. Some, but not all, allyl sulfur compounds can also effectively retard tumor proliferation and induce apoptosis. Changes in cellular thiol and phosphorylation stains may account for some of these antitumorigenic properties. The anticarcinogenic potential of garlic can be influenced by several dietary components including specific fatty acids, selenium, and vitamin A. Since garlic and its constituents can suppress carcinogen formation, carcinogen bioactivation, and tumor proliferation it is imperative that biomarkers be established to identify which individuals might benefit most and what intakes can occur with ill consequences[19].

Anti-leukemic effects

The organosulfur compound ajoene, a constitutent of garlic, has been shown to induce apoptosis in a leukemic cell line as well as in blood cells of a leukemic patient. It shows here that ajoene

(20 microM) leads to a time-dependent activation of caspase-3-like activity as well as to the proteolytic processing of procaspase-3 and -8. These results indicate that apoptosis in leukemia cells triggered by ajoene is based on the activation of a mitochondria-dependent caspase cascade which includes also the activation of the initiator caspase-8[20].Several garlic compounds including allicin and its corresponding sulfide inhibit the proliferation and induce apoptosis of several human non-leukemia malignant cells including breast, bladder, colorectal, hepatic, prostate cancer, lymphoma and skin tumour cell lines. Ajoene (4,5,9 trithiadodeca-1 6,11-triene-9-oxide) is a garlic derived compound produced most efficiently from allicin and has the advantage of a greater chemical stability than allicin. Several clinical trials and in vitro studies of ajoene have demonstrated its best-known anti-thrombosis, anti-microbial and cholesterol lowering activities. Recently, topic application of ajoene has produced significant clinical response in patients with skin basal cell carcinoma. Ajoene was shown to inhibit proliferation and induce apoptosis of several human leukaemia CD34-negative cells including HL-60, U937, HEL and OCIM-1. Also, ajoene induces 30% apoptosis in myeloblasts from chronic myeloid leukemia patient in blast crisis.

Immunomodulatory effects

Using various kinds of models, we examined the effects of aged garlic extract (AGE) on immune functions. In the immunoglobulin (Ig) E-mediated allergic mouse model, AGE significantly decreased the antigen-specific ear swelling induced by picryl chloride ointment to the ear and intravenous administration of antitrinitrophenyl antibody. In the transplanted carcinoma cell model, AGE significantly inhibited, the growth of Sarcoma-180 (allogenic) and LL/2 lung carcinoma. (syngenic) cells transplanted into mice. Concomitantly, increases in natural killer (NK) and killer activities of spleen cells were observed in sarcoma-180 bearing mice administered AGE. In psychological stress model, AGE significantly prerented the decrease in spleen weight and restored the reduction of anti-SRBC hemolytic. Plaque-forming cells caused by the electrical stress. These studies strongly suggest that AGE could be a promising candidate as an immune modifier, which maintains the homeostasis of immune functions; further studies are warranted to determine when it is most beneficial. [21]. Allicin, the immunologically active component of garlic, has been found to affect oxidative stress and immune response in several experimental systems.

Garlic can detoxify carcinogens by stimulation of cytochrome P (450) enzymes, antioxidant activity or sulfur compound binding. Studies demonstrate a direct toxic effect of garlic' to sarcoma and gastric, colon, bladder and prostate cancer cells in tissue culture, but these effects cannot explain the inhibition of growth of transplanted cancer in animal models. Clinical trials should be initiated to test the hypothesis that the immune stimulation arid other beneficial effects of garlic are able to reduce the incidence of cancer. [22].

Antidiabetic effect

It is investigated the effects of garlic oil and diallyl disulfide (DADS) on glycemic control and renal function, in rats with streptozotocin-induced diabetes. Rats received by gavage garlic oil (100mg/kg body wt) or DADS (40 or 80mg/kg body wt) every other day until 16weeks after the induction of diabetes. The control rats were treated with corn oil only, neither garlic oil nor DADS. Garlic oil did not affect oral glucose tolerance in diabetes acutely but significantly improved oral glucose tolerance, at 4, 8. 12, and l6 weeks and significantly ameliorated proteinuria at the end of l6 weeks: DADS did not significantly affect oral glucose tolerance or renal function, Diabetic rats fed, 80mg DADS/kg body Wt had a significantly lower rate of body weight gain and a significantly lower ratio of muscle weight to body weight. In conclusion, long term treatment of diabetes with garlic oil can improve oral glucose tolerance and renal function in diabetes but not through the action of DADS. [23] Garlic administration significantly improved the impaired endothelium-dependent relaxations and decreased the enhanced contractile response to phenylephrine in diabetic rats. It is concluded that intraperitoneal administration of aqueous garlic can improve endothelial dysfunction in insulin-dependent model of diabetes [24]

Antiglycation1properties

Diabetes mellitus is a common endocrine disorder affecting the eyes, nerves, blood vessels, skin, and kidneys. Increased glycation of proteins, accunulation of advanced glycation endproducts (AGEPs) have been implicated in the pathogenesis of diabetic complications. Glycation and AGEP formation are also accompanied by formation of free radicals via autoxidation of glucose. Compounds with combined antiglycation and antioxidant properties offer therapeutic potential. Recent studies suggest that garlic extract inhibits formation of AGEPs in vitro a key component of aged garlic is a potent antioxidant and can inhibit AGEP formation [25].

Cardiovascular Effects

Chronic oral administration of garlic administration prevents acute adriamycin-induced cardiotoxicity and decreases myocardial TNF-alpha expression. [26] The GUSTO angiographic trial helps to confirm the open artery theory. Cholesterol levels in US adults continue to decrease. The consumption of one-half to one clove of garlic per day reduces cholesterol levels by approximately 9%. [27] Recently there has been renewed interest in its role in the treatment of cardiovascular disease and its effectiveness in offsetting the risks of such conditions. The results of numerous studies are showed that garlic can bring about plasma lipids normalization, enhancement of fibrinolytic activity, inhibition of platelet aggregation and reductions in blood pressure and blood glucose. It is concluded that garlic has potential in the prevention and control of cardiovascular disorders. [28]

Phytoestrogenic efficacy:

The present studies was undertaken to exam effects of an oil extract of garlic on the intestinal transference of calcium and also to verify its role in maintaining the bone content and bone tensile strength ovariectomized rat model of osteoporosis. The results of this study propose that the phytoestrogenic efficacy of an oil extract of garlic prevents ovarian hormone deficiency bone mineral loss possibly by promoting intestinal transference of calcium through the partial revival of the serum estrogen titer. [29]

Preventing the common cold

One hundred forty-six volunteers were randomized to receive a placebo or an allicin-containing garlic supplement, one capsue daily, over a 12-week period between November and February. They used a five-point scale to assess their health and recorded any common cold infections and symptoms in a daily diary. The active-treatment group had significantly fewer colds than the placebo group (24 vs 65, $P < .001$). The placebo group, in contrast, recorded significantly more days challenged virally (366 vs 111, $P < .05$) and a significantly longer duration of symptoms (5.01 vs 1.52 days, $P < .001$). Consequently, volunteers in the active group were less likely to get a cold and recovered faster if infected. Volunteers taking placebo were much more likely to get more than one cold over the treatment period. An allicin containing supplement can prevent attack by the common cold virus. [30]

Analgesic activity

Ethanol (70%) extract of fresh bulb administered intraperitoneally to mice of both sexes at variable dosage levels was active. [31]

Anti-amebic activity

Essential oil in broth culture concentration of 2.0 µ/ml was active on *Entamoeba histolytica*. [32]

Anti-ascariasis activity

Ethanol (95%) extract of bulbs when applied externally was active on earthworms. Paralysis occurred in 12 hours with death of 50% of the worms. [33] Water extract applied externally to earthworms at a concentration of 10mg/ml produced strong activity [34]

Toxicity effects

The influence of garlic extract on the chronic toxicity test were examined orally in Wistar rats for 6 months. There were no toxic symptoms due to garlic extract even at dose level of 2000 mg/kg for 5 times a week during 6 months. High dose of garlic extract did not inhibit the body weight gain, while the food consumption decreased slightly for the nutritional effects of it in both male and female rats. There were no significant differences in urinary, hematological and serological examinations compared each groups. In the histopathological findings, no toxic signs were observed on any of the tissues and organs examined. [35]

REFERENCES

1. Nandan Kumar Jha, Allium sativum: galic :Lashoon, Phytopharm, 2006,7(8);3-24
2. Hemadri.K, Sasibhushana rao.S, Ancient Sd. Life 1983; 3(2): 103 -107.
3. Hikino,H, Aota.k, Takemoto.T, Chem Pharma Bull. 1966; 14: 890.
4. Chopra.P.N, Indigenous drugs of India, Their medical and EconomicAspects,The Art Press, Calcutta. India. 1933; 550
5. Reddy.M.B., Reddy.KR, Reddy.M.N, Int. J Crude drug Res. 1989; 27(2):185 -189.
6. Lal.S.D, Yadev.BK, Econ Bot. 1983; 37(3): 299 -305.
7. Kamboj.V.P, Indian J Med. Res. 1988; 4: 336 -355.
8. Bourre.JM, J Nutr Health Aging. 20C5 Nov-Dec; 9(6):421-32.
9. Bedjer.TM, Bonis.MJ, J Nutr 2002 Mar; 131(3s):1 106S-8S
10. Undergraduate Special Project Report. Fac Pharm Mahidol Univ. Bangkok 1975; l09.
11. Ungsurungsie.M,Suthienkul.O, Paovalo.C, Food Chem. Toxicol. 1982; 20: 527 -530.

12. Morioka, N., LL Sze, DL Morton and RF Irie, J Ethnopharmacol. 1993; 39(2): 119-128.
13. Razzack, HMA, Fitoterapia 1980; 51: 201 —205.
14. Ramnath Chopra, HerbaPol. 1980; 26(4): 245 —250.
15. Costa, M., LC di Stasi, M. Kirizawa , SLJ Mendacolli, C. Gomez, and G. Trolin. Ethnopharmacol 1987; 20(3): 223 —237.
16. Dawit Dikasso, Hirut Lemma, Kelbessa Urga, Asfaw Debella, Getachew Addis, Ashenif Tadele, Kidist YirsawEthiop Med J. 2002 JuI;40(3):241-9
17. Ritland SR, Leighton JA, Hirsch RE, Morrow JD, Weaver AL, Gendler SJ. Nutr Cancer 2000; 38(2) :255-64
18. Rahman K J Nutr 2001 Mar; 131(3s): p977S-9S
19. Leal PF, Braga ME, Sato DN, Carvalho JE, Marques MO, Meireles MA. J Nutr 2001 Mar; 131(3s): 1010S-5S.
20. Dirsch VM, Antlsperger DS, Hentze.H, Vollmar.A.M, Leukemia 2002 Jan;16(1):74-83
21. Yeb.YY, Lie.L, .JNutr20*0l* Mar; 131(3s):989S-983S
22. Gerritsen, J Nutr 2001 Mar; 1 31(3s): 1 067S-70S
23. Chowthry R, Datta.A, Food Chem Toxicol. 2006 Aug; 44(8):1377-84
24. Lie.RW, Davin Lin. G, J EthnopharmacoL 2003 Mar, 85(1): 139-44
25. Der Marderosian A, J Nutr. 2006 Mar; 136(3 Suppl): 782S-788S.
26. Bradford, MM BMC Pharmacol. 2003 Dec 20; 3’16
27. Warshafsky S, Kamer RS, Sivak SL, JAMA 1994 Jun 1; 271:1660-1661
28. Ernst E, Pharmatherapeutica 1987; 5(2): 83-9
29. Gurley BJ, Barone GW, Williams DK, Carrier J, Breen P, Yates CR,Phytother Res. 2006 May;20(5):408-15.
30. Winkler P, de Vrese M, Laue Ch, Schrezenmeir J. *Adv TImer* 2001 Jul-Aug; 18(4): 189-93
31. Chang, HM, TC Chiang and CW Mak, Fitoterapia 1982; 53: 147-162
32. Filipoy, A., J Toxicol Clin Exp. 1990: 10 (6): 361-373
33. Kayeysa raj.R,Indian J Physiol. Pharmacol 1975; 19: 47-49.
34. Boca Raton, J Sci. lnd. Res. 1960; C19: 202.
35. Nakagawa S,J Toxicol Sci 1984 Feb;9(1):61-75.