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Garlic: A Boon for Oral Diseases

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Abstract

The garlic also known as Allium sativum. Garlic and onions are originally native to central Asia and are among the oldest cultivated plants in the world Garlic has attracted particular attention of modern medicine because of widespread belief about its effects in maintaining good health. It is part of a monocot genus of flowering plants frequently referred to onion genus. The genus includes approximately 500 species [4] including edible onions (A. cepa), garlics (A. sativum), shallots (A. ascalonicum), chives (A. schoenoprasum), and leeks (A. porrum). Chemically garlic contains many active therapeutic components which are widely studies.Garlic has anticariogenic, anti-oxident, antibacterial, antifungal properties and many more. This review presents the scope and therapeutic application of garlic in oral diseases and dentistry.

Keywords: Allium; Medicinal Plants; Garlic**.**

Historical Perspective

The garlic has been used throughout the world as a medicine since last thousands of years. The use of garlic as remedy has been described in Sanskrit literature. The Latin name of garlic is allyl. Theodor Wertheim, a German chemist (1844), have distilled a pungent substance from garlic and named it allyl. Louis Pasteur(1848) in Paris showed that allyl could inhibit the growth of bacteria. The Babylonians, Egyptians, Phoenicians, Vikings, Chinese, Greeks, Romans and Hindus have used garlic for different therapeutic purposes. Garlic was used as a remedy for intestinal disorders, flatulence, worms, respiratory infections, skin diseases, wounds, aging and other diseases [1].

Some of the earliest references for therapeutic application of garlic were found in Avesta, a collection of Zoroastrian holy writings that was probably compiled during the sixth century [1]. During the earliest Olympics in Greece, garlic was fed to the athletes for increasing stamina [2]. The Indian and Ancient Chinese medicine recommended garlic to aid in respiration and digestion.Garlic is also used to treat leprosy and parasitic infections [3]. Al Qanoon Fil Tib (The Canon of Medicine) written by Avicenna in 1988 recommended garlic as a useful therapeutic compound in treatment of arthritis, toothache, chronic cough, constipation, parasitic infestation, snake and insect bites, gynecologic diseases as well as in infectious diseases. Garlic has attracted particular attention of modern medicine because of widespread belief about its effects in maintaining good health. Allium is the Latin word for garlic. It is part of a monocot genus of flowering plants frequently referred to onion genus. The genus includes approximately 500 species [4] including edible onions (A. cepa), garlics (A. sativum), shallots (A. ascalonicum), chives (A. schoenoprasum), and leeks (A. porrum). Garlic and onions are originally native to central Asia and are among the oldest cultivated plants in the world [4]. Garlic's edible bulbs are an important culinary spice and constituent of traditional Chinese medicine. The allium has been valued in many cultures for their pungent flavours and culinary uses and for their health benefits for over 4000 years [5,6]. Ancient medical texts from Egypt, Greece, Rome, China, and India cite therapeutic applications for Allium vegetables [5]. An Egyptian medical papyrus,The Codex Ebers (~1550 B.C.) lists

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22 preparations in which garlic was added. Hippocrates advocated garlic as a laxative and a diuretic and Aristophanes and Galenal suggested garlic for the treatment of uterine tumors [6].

Chemical Composition of Garlic

The chemistry of garlic is quite complex. It's clinical and pharmacological properties have been extensively studied. Whole garlic cloves are intact bulbs that contain an odorless, sulfur-containing amino acid derivative. The primary sulfur-containing constituents in whole intact garlic is glutamyl 7 cysteines and S allyl cysteine sulfoxides including alliin. When the bulb is crushed or cut, alliin is altered by the enzyme, alliinase and is converted into allicin. Allicin is an oily, yellow liquid that gives garlic its characteristic odor. Typical volatiles in crushed garlic and garlic essential oil include diallyl sulfide (DAS), diallyl disulfide (DADS), diallyl trisulfide, methyl allyl disulfide, methyl allyl trisulfide, 2- vinyl-1,3-dithiin, 3-vinyl-1,2-dithiin and ajoene [6,7]. When crushed, Allium sativum yields allicin, a powerful antibiotic and antifungal compound. It also contains the sulfur containing compounds alliin, ajoene, diallylsulfide, dithiin, S-allylcysteine, enzymes, vitamin B, proteins, minerals, saponins, flavonoids and maillard reaction products which are non-sulfur containing compounds. Phytoalexin is also called allixin has anti-oxidative effects, antimicrobial effects, anti-tumor promoting effects, inhibition of aflatoxin B2 DNA binding and neurotrophic effects [8-10]. Sulfur- and non-sulfur-containing chemical constituents have been isolated from Bulbus Allii Cepae.The sulphur compounds are the most characteristic. The organic sulphur compounds of Bulbus Allii Cepae including the thiosulfinates, thiosulfonates, cepaenes, S-oxides, dioxides, monosulfides, disulfides, trisulfides and zwiebelanes occur only as degradation products of the naturally occurring cysteine sulfoxides [11]. Fresh garlic contains water, carbohydrates, proteins, fiber, fat as well as essential amino acids, vitamins and minerals. When garlic is cut, chopped or crushed, the clove's membrane is disrupted and S-allylcysteine sulfoxide is transformed enzymatically into allicin by alliinase [11]. Allicin is responsible for the typical odor of garlic but it is unstable and converts readily into mono, di and trisulfides and other compounds such as ajoene.

Allicin is an organo sulfur compound obtained from garlic, a species in the family Alliaceae. Allicin features the thiosulfinate functional group, R-S(O)-S-R. The compound is not present in garlic unless tissue damage occurs and is formed by the action of the enzyme alliinase on alliin. Allicin begins to break down quickly expecially if heated. Conversely its breakdown can be slowed by refrigeration [12]. It was first isolated and studied in the laboratory by Chester J. Cavallito in 1944 [13]. This compound exhibits antibacterial and anti-fungal properties [13].

Onions mainly contain S-propenylcysteine sulfoxide [11] but also other sulfoxides, including S-propylcysteine sulfoxide and S-methylcysteine sulfoxide [14]. S-Propenylcysteine sulfoxide, positional isomer of alliin, is called lacrimatory precursor, because it is transformed by alliinase into the lacrimatory factor propanethial S-oxide. The lacrimatory factor is highly reactive and hydrolyzes to propionaldehyde, sulfuric acid and hydrogen sulphide. It is also the precursor of several sulfur derivatives. Organosulfur compounds present in Allium vegetables which are either lipid or water soluble are considered responsible for the beneficial effects of these herbs. Garlic derivatives generally have a thioallyl moiety whereas onion extracts contain a thiopropyl group with somewhat different chemical properties. Further transformation of organo sulfur compounds can occur after interaction with free sulfhydryl groups including those present in cysteine, glutathione or proteins [15,16]. Incubation of cystein with allyldisulfide or diallylsulfide groups produces S-allylmercaptocysteine and allylmercaptane respectively [17]. S-Allylmercaptocysteine is further transformed to allylmercaptane following incubation with fresh blood. One study [18] in the isolated, perfused rat liver showed that allicin is first metabolized to diallyldisulfide which is further reduced to allylmercaptane. Another study identified allylmercaptane and allylmethylsulfide as metabolites of diallyldisulfide and diallylsulfidein primary rat hepatocytes [19]. Urine from healthy individuals consuming garlic or onions contains N-acetyl-S-allylcysteine and N-acetyl-S-(2-carboxylpropyl)-cysteine [20-22]. Allylmercaptane and diallyldisulfide have been found in human breath after ingestion of garlic [23,24]. Allium Vegetables contain similar quantities of many nutrients, particularly macronutrients though garlic is a richer source of many minerals, including selenium. Onions, because they are consumed in larger quantities than other Allium vegetables are a more significant dietary source of carbohydrates, fiber, potassium, iron, and vitamin C [25]. Allium vegetables contain a variety of bioactive compounds including flavonoids, oligosaccharides, arginine, and selenium [26] however much of Allium's health benefits and the majority of studies on them focus on their sulfur-containing components [26,27]. In fact, sulfur comprises approximately 1% of the dry weight of garlic [28] and up to 0.5% of the dry weight of onions

[29]. Sulfur-containing compounds in garlic are largely derived from the precursors γ-glutamyl-S-alk(en)yl-L-cysteines and S-alk(en)yl-L-cysteine sulfoxides [30]. Alliin S-allylcysteine sulfoxide is the major ASCO found in garlic [30]. Upon damage or crushing of the vegetable bulbs, the enzyme alliinase is released from the vacuoles of cells and catalyzes the cleavage of ASCOs to sulfenic acid intermediates [31]. The intermediates are highly reactive and rapidly produce thiosulfinate compounds via condensation reactions. The major garlic thiosulfinate produced is allicin. Allicin and its oil-soluble metabolites are largely responsible for garlic's odor. Allicin is unstable and breaks down further to ajoene, vinyldithiins and sulfides including diallyl sulfide (DAS), diallyl disulfide (DADS) and diallyl trisulfide (DATS) [27,32-34]. In onions, cleavage of isoalliin and other precursor compounds and the subsequent condensation of the sulfenic acid intermediates results in the formation of lachrymatory factor (thiopropanal S-oxide) and in thiosulfonates, bis-sulfines, sulfides including DAS, DADS, and DATS; zweiebelanes, and cepaenes, all of which contribute to the flavor of onions [27, 30,35].

Uses in Oral Diseases

Oesophageal Cancer

Chen et al found that consumption of raw garlic at least one time per week was associated with reported incidence of 0.2% of esophageal cancer in Taiwanese men. The Italian and Swiss case-control study also reported that consumption of ≥7 portions of garlic per week was protective against esophageal cancer and that increasing garlic intake was protective [36]. The WCRF/AICR report reviewed one cohort and eight case-control studies that assessed the effect of garlic, onions or Allium vegetables collectively on risk of esophageal cancer [37]. Only one of the case-control studies showed a statistically significant decrease in risk. Substantial evidence indicates that garlic extracts can inhibit a range of Gram-negative and Gram-positive bacteria and serve as antifungal agents [38]. Various sulfur compounds including allicin, DAS, DADS, and ajoene derivatives may contribute to garlic's antimicrobial properties [39]. Garlic's inhibitory effect against the bacteria Helicobacter pylori is of note as H. pylori colonization of the gastric mucosa is linked with gastritis and a greater propensity to develop gastric cancer. Cellini et al [40] demonstrated that aqueous garlic extracts (2–5 mg/ml) inhibited H. pylori proliferation. Both DAS and DADS elicited a dose dependent depression in H. pylori proliferation in culture [41]. Raw garlic extracts and three commercially available garlic tablets varied in their efficacy against H. Pylori as indicated by minimum inhibitory concentrations in the range between 10 to 17.5 μg dry weight/ml [42]. The ability of garlic to reduce H. pylori infection in humans is inconclusive. While an epidemiological study suggested an association between increased garlic consumption and reduced H. pylori infection [43]. Two clinical studies that tested different garlic preparations in H. pylori infected subjects did not show efficacy [44,45]. Neither of these interventions resulted in the elimination of the organism, change in the severity of gastritis or a significant change in symptom scores. Both studies were not randomized and had small sample sizes suggesting that a well-designed clinical trial is still needed to determine the efficacy of garlic consumption in reducing H. pylori infection and symptoms.

The primary antimicrobial effect of garlic may reflect chemical reactions with selected thiol groups of enzymes and/or a change in the overall redox state of the organism. Specifically the antimicrobial action of allicin and its breakdown products has been suggested to be due to its rapid interaction with SH-containing molecules including amino acids and cellular proteins within microbial organisms [46]. Changes in thiol status have been suggested as one possible mechanism by which garlic and related sulfur compounds might also suppress tumor proliferation.

Anticariogenic

In one study done in Bapuji dental college and hospital, Davangere, Karnataka, India, it was concluded that garlic mouth wash is significantly active against streptococcus mutans and lactobacilli and found that garlic significantly reduced bacterial count on 14th day even after discontinuation of mouthwash on 7th day [47]. In an in vitro study [48] inhibitory activity of garlic extracts on multidrug - resistant (MDR) strains of Streptococcus mutans isolated from human carious teeth was assessed all isolates MDR and non MDR of S mutans were sensitive to garlic extracts with the MIC ranging from 4 - 32μgml [7]. Garlic cloves can be used as a remedy for fungal infections such as oral thrush [49].

Antibacterial and Antifungal

Allium sativum, commonly known as garlic, is one of suggested alternatives to antibiotics with antibacterial effects against a wide range of bacteria including Escherichia, Lactobacilli, Helicobacter

pylori, Pseudomonas aeruginosa, Klebsiella pneumonia and Mycobacterium tuberculosis [50-55]. Streptococcus mutans are responsive to garlic extract with the minimum inhibition concentration ranging from 4 to 32 μg/ml [56]. Garlic extract was sensitive particularly to P.gingivlais, P.Intermedia, A. actinomycetemcomitans, F. Nucleatum and had lower minimum inhibitory concentration (MICs) and minimum bactericidal concentration (MBCs) than the other gram negative organisms tested. Trypsin like activity and total protease activity are almost completely inhibited by garlic extract, apparently through allicin's affinity for thiol groups [57]. Bakri IM et al confirmed the antifungal activity of garlic 12 against C. albicans described by Ghannoum MA. Ledezma [58] et al demonstrated that ajoene, an active compound in garlic may play a role as a topical fungal agent.

Aphthous Ulcer

The major component of garlic is allicin, which could effectively decrease inflammatory factors secretion, reduce the migration of neutrophils, inhibit bacterium and virus, antagonize oxidation and regulate immunity. By these bioactivities of anti-inflammation, anti-microbial activity, anti-oxidation and immunomodulation, the allicin may be an effective therapeutic candidate to control the pain, promote ulcer healing and prevent the recurrence of RAU [59].

Herpes Simplex Virus Infection

Fresh garlic extracts in which allicin is known to be the main active component have been shown to have in vitro and in vivo antiviral activity. The viruses that are sensitive to garlic extracts are the human cytomegaloviruses and herpes simplex virus type1 [60].

Anti Oxidant Properties

Abundant research has established garlic and its organosulfur compounds to be strong antioxidants. Garlic protection against oxidant induced damage can be Credited to major compounds in garlic extract like Sallycysteine (SAC) and S-allylmercapto-L-cysteine, by displaying radical scavenging activity and modulating cellular antioxidant enzyme activity [61].

Oral Cancer

The chemoprotective effect of garlic oil on 7, 12-dimethylbenzanthracene (DMBA) induced carcinogenesis in sub-maxillary salivary glands of male wistar rats was studied. There is evidence from the study that betacarotene can indeed function as a non-conventional antioxidant at low oxygen pressures and thus render protection against cancer by preventing lipid peroxidation in vivo [62]. In a 7, 12-dimethylbenz[a]anthracene (DMBA)-induced hamster buccal pouch carcinogenesis model, water extracts of fresh garlic induced apoptosis of malignant cells and completely prevented the onset of oral carcinoma [63]. Inhibition of nitrosamines and heterocyclic amines—Nitrosamines and heterocyclic amines (HCA) are potential dietary carcinogens which are not normally present in foods but may arise during preservation or cooking [64]. Evidence points to the ability of allyl sulfur compounds to suppress the spontaneous and bacterial mediated formation of nitrosamines [65], although not all allyl sulfur compounds prevent nitrosamine formation equally. SAC and its analog S-propyl cysteine, but not DADS, dipropyl disulfide, or DAS, retarded nitrosamine formation, suggesting a critical role for a cysteine residue in inhibition [66]. Further, water extracts of garlic, deodorized garlic powder, and onion, but not leeks, decreased nitrosamine formation [66]. The reduction in nitrosamine formation may be a result of increased formation of nitrosothiols, as sulfur compounds might reduce nitrite availability for nitrosamine formation [67]. In humans, ingesting 5 g of garlic per day completely blocked the enhanced urinary excretion of nitrosoproline, an indicator for the synthesis of potentially carcinogenic nitrosamines, that occurred as a result of ingesting supplemental nitrate and proline [68]. More recent evidence suggests that as little as 1 g of garlic may be sufficient to suppress nitrosoproline formation [69].

Warts

In a preliminary trial, topical application of garlic cloves was used successfully to treat warts in a group of children. A clove was cut in half each night and the flat edge of the clove was rubbed onto each of the warts, carefully cleaning the surrounding areas, so as not to spread any garlic juice. The areas were covered overnight with Band-Aids or waterproof tape and were washed in the morning. In all cases, the warts cleared completely after an average of 9 weeks after an average of nine weeks [70,71].

Anti protozoal Properties

Several studies have shown that the extract was effective against a host of protozoa including Candida

albicans [72], Scedosporium prolificans [73], tinea pedis [74], Opalina ranarum, Balantidium entozoon, Entamoeba histolytica, Trypanosomes, Leishmania, Leptomonas, and Crithidia [75]. Due to the occurrence of unpleasant side effects and increasing resistance to the synthetic pharmaceuticals, garlic was recommended for the treatment of giardiasis. Inhibitory activity of garlic on giardia was noted with crude extract at 25 pg/mlL and the lethal dosage was established as approximately 50 pg/mL. Encouraged by these results, a clinical trial was carried out on patients that had giardiasis [76]. Garlic was established as an antigiardial, removing the symptoms from all patients within 24 h and completely removing any indication of giardiasis from the stool within 72 h at a dosage of 1 mg/mL twice daily aqueous extract or 0.6 mg/mL commercially prepared garlic capsules.

Adverse Effects of Garlic

Case reports have highlighted the possibility that garlic use may cause allergic reactions (allergic contact dermatitis, generalized urticaria, angiedema, pemphigus, anaphylaxis and photoallergy), alteration of platelet function and coagulation {with a possible risk of bleeding) and burns (when fresh garlic is applied on the skin, particularly under occlusive dressings). It causes Heartburn and flatulence.Because of garlic's anti-clotting properties, people taking anticoagulant drugs should check with their doctor before taking garlic. Those scheduled for surgery should inform their surgeon if they are taking garlic supplements [77]. Garlic should not be taken during pregnancy since it has abortifacient properties. It should also be avoided during lactation as it has been shown to enter breast milk, altering the odour of the milk and affecting the suckling behaviour of the infant [78]. Garlic is known for causing halitosis as well as causing sweat to have a pungent 'garlicky' smell which is caused by Allyl methyl sulfide (AMS). AMS is a gas which is absorbed into the blood during the metabolism of garlic; from the blood it travels to the lungs (and from there to the mouth causing bad breath) and skin where it is exuded through skin pores. Washing the skin with soap is only a partial and imperfect solution to the smell.Raw garlic is more potent and therefore cooking garlic reduces the effect [79,80]. Increased bacterial biofilm formation on orthodontic wire [81] were reported when garlic extract used as a mouth wash [81]. Finally, garlic may enhance the pharmacological effect of anticoagulants (e.g. warfarin, fluindione) and reduce the efficacy of anti-AIDS drugs (i. e. saquinavir) [82].

Conclusion

As the medicine is moving towards use of more herbal products, due to its vast therapeutic potential the garlic can be utilized as herbal medicine for treatment of many oral diseases and other medical conditions. However more research studies are needed to explore this herbal medicine.

References

1. Dannesteter J. AVESTA: VENDIDAD: Fargard 20: The origins of medicine.Translated from Sacred Books of the East, American Edition. New York: The Christian Literature Company.2003.
2. Lawson LD, Bauer R. Garlic: a review of its medicinal effects and indicated active compounds. In: Phytomedicines of Europe. Chemistry and Biological Activity. Series 69 1. Washington DC: American Chemical Society.1998. p. 176–209.
3. Rivlrn RS. Patient with hyperlipidemia who received garlic supplements Lipid management. Report from the Lipid Education Council. 1998; 3:6–7.
4. Guercio V, Galeone C, Turati F, La Vecchia C. Gastric cancer and allium vegetable intake: a critical review of the experimental and epidemiologic evidence. Nutrition and cancer. 2014; 66:757–73.
5. Milner JA. Garlic: its anticarcinogenic and antitumorigenic properties. Nutrition reviews. 1996; 54:S82–6.
6. Sengupta A, Ghosh S, Das S. Modulatory influence of garlic and tomato on cyclooxygenase-2 activity, cell proliferation and apoptosis during azoxymethane induced colon carcinogenesis in rat. Cancer letters. 2004; 208:127–36. [PubMed: 15142670].
7. Block E. The chemistry of garlic and onions. Sic Am 1985; 252: 114-119.
8. WHO Monographs on Selected Medicinal Plants. Geneva: Availablefromhttp://apps.who.int/medicinedocs/documents/s14213e/s14213e.pdf [Updated 2012 April 24;cited 2012 May 25].
9. True star health.com. Truestar Health & Healthnotes, Inc., [cited 2012May25].Availablefrom http://www.truestarhealth.com/Notes/2093008.html.
10. Wikipedia.org. Wikimedia Foundation, Inc., [Updated 2012 May 24; cited 2012 May 25]. Available from http://en.wikipedia.org/wiki/onion.
11. Block E. The chemistry of garlic and onions. Sci Am. 1985; 252:94–99.
12. Eric Block. "The chemistry of garlic and onions". Scientific American 1985; 252:114–19.
13. Cavallito CJ, Bailey JH, "Allicin, the Antibacterial Principle of Allium sativum. I. Isolation, Physical

Properties and Antibacterial Action. J Am Chem Soc 1944; 66:1950-51.

14. Virtanen AL, Matikkala EJ. The isolation of S-methyl-Lcysteine sulphoxide and S-n-propyl-L-cysteine sulphoxide from onion (Allium cepa) and the antibiotic activity of crushed onion. Acta Chem Scand.1976; 13:1898–1900.
15. Weisberger AS, Pensky J. Tumor inhibition by a sulfhydryl-blocking agent related to an active principle of garlic (Allium sativum). Cancer Res. 1958; 18:1301–1308.
16. Gilbert HF. Molecular and cellular aspects of thiol-disulfide exchange. Adv Enzymol Relat Areas Mol Biol.1990; 63:69–172.
17. Lawson LD, Wang ZJ. Pre-hepatic fate of the organosulfur compounds derived from garlic (Allium sativum).Planta Med. 1993; 59:A688–A689.
18. . Egen-Schwind C, Eckard R, Kemper FH. Metabolism of garlic constituents in the isolated perfused rat liver.Planta Med.1992; 58:301–305.
19. Sheen LY, Wu CC, Lii CK, Tsai SJ. Metabolites of diallyl disulfide and diallyl sulfide in primary rat hepatocytes.Food Chem Toxicol.1999; 37:1139–1146.
20. Jandke J, Spiteller G. Unusual conjugates in biological profiles originating from consumption of onions and garlic.J Chromatogr.1987; 421:1–8.
21. de Rooij BM, Boogaard PJ, Rijksen DA, Commandeur JN,Vermeulen NP. Urinary excretion of N-acetyl-S-allyl-Lcysteine upon garlic consumption by human volunteers.Arch Toxicol.1996; 70:635–639.
22. de Rooij BM, Boogaard PJ, Commandeur JN, van Sittert NJ, Vermeulen NP. Allylmercapturic acid as urinary biomarker of human exposure to allyl chloride. Occup Environ Med.1997; 54:653–661.
23. Laakso I, Seppanen-Laakso T, Hiltunen R, Muller B, Jansen H, Knobloch K. Volatile garlic odor components:gas phases and adsorbed exhaled air analysed by headspace gas chromatography-mass spectrometry. Plant Med.1989; 55:257–261.
24. Minami T, Boku T, Inada K, Morita M, Okazaki Y. Odor components of human breath after the ingestion of grated raw garlic. J Food Sci.1989; 54:763–765.
25. U.S. Department of Agriculture, Agricultural Research Service. USDA National Nutrient Database for Standard Reference, Release 24. Nutrient Data Laboratory Home Page. 2011. http://www.ars.usda.gov/ba/bhnrc/ndl.
26. Milner JA. Preclinical perspectives on garlic and cancer. The Journal of nutrition. 2006; 136:827S–31S.
27. Block E. The chemistry of garlic and onions. Scientific American. 1985; 252:114–9.
28. Fenwick GR, Hanley AB. The genus Allium—Part 3. Critical reviews in food science and nutrition. 1985; 23:1–73.
29. Lee EJ, Yoo KS, Jifon J, Patil BS. Characterization of shortday onion cultivars of 3 pungency levels with flavor precursor, free amino acid, sulfur, and sugar contents. Journal of food science. 2009; 74:C475–80.
30. Kubec R, Svobodova M, Velisek J. Gas chromatographic determination of S-alk (en)ylcysteine sulfoxides. Journal of chromatography A. 1999; 862:85–94.
31. Lanzotti V. The analysis of onion and garlic. Journal of chromatography A. 2006; 1112:3–22.
32. Lawson LD, Wang ZJ, Hughes BG. Identification and HPLC quantitation of the sulfides and dialk(en)yl thiosulfinates in commercial garlic products. Planta medica. 1991; 57:363–70.
33. Lawson LD, Wood SG, Hughes BG. HPLC analysis of allicin and other thiosulfinates in garlic clove homogenates. Planta medica. 1991; 57:263–70.
34. Tamaki T, Sonoki S. Volatile sulfur compounds in human expiration after eating raw or heat-treated garlic. Journal of nutritional science and vitaminology. 1999; 45:213–22.
35. Griffiths G, Trueman L, Crowther T, Thomas B, Smith B. Onions—a global benefit to health. Phytotherapy research : PTR. 2002; 16:603–15.
36. Galeone C, Pelucchi C, Levi F, Negri E, Franceschi S, Talamini R, et al. Onion and garlic use and human cancer. The American journal of clinical nutrition. 2006; 84:1027–32.
37. World Cancer Research Fund / American Institute for Cancer Research. Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. Washington DC: AICR; 2007.
38. Adetumbi MA, Lau BH. Allium sativum (garlic)—a natural antibiotic. Medical hypotheses. 1983; 12: 227–37.
39. Tsao SM, Yin MC. In-vitro antimicrobial activity of four diallyl sulphides occurring naturally in garlic and Chinese leek oils. Journal of medical microbiology. 2001; 50:646–9.
40. Cellini L, Di Campli E, Masulli M, Di Bartolomeo S, Allocati N. Inhibition of Helicobacter pylori by garlic extract (Allium sativum). FEMS immunology and medical microbiology. 1996; 13:273–7.
41. Chung JG, Chen GW, Wu LT, Chang HL, Lin JG, Yeh CC, et al. Effects of garlic compounds diallyl sulfide and diallyl disulfide on arylamine N-acetyltransferase activity in strains of Helicobacter pylori from peptic ulcer patients. The American journal of Chinese medicine. 1998; 26:353–64.
42. Jonkers D, van den Broek E, van Dooren I, Thijs C, Dorant E, Hageman G, et al. Antibacterial effect of garlic and omeprazole on Helicobacter pylori. The Journal of antimicrobial chemotherapy. 1999; 43:837–9.
43. You WC, Zhang L, Gail MH, Ma JL, Chang YS, Blot WJ, et al. Helicobacter pylori infection, garlic intake and precancerous lesions in a Chinese population at low risk of gastric cancer. International journal of

epidemiology. 1998; 27:941–4.

44. Aydin A, Ersoz G, Tekesin O, Akcicek E, Tuncyurek M. Garlic oil and Helicobacter pylori infection. The American journal of gastroenterology. 2000; 95:563–4.
45. Graham DY, Anderson SY, Lang T. Garlic or jalapeno peppers for treatment of Helicobacter pylori infection. The American journal of gastroenterology. 1999; 94:1200–2.
46. Davis SR. An overview of the antifungal properties of allicin and its breakdown products—the possibility of a safe and effective antifungal prophylactic. Mycoses. 2005; 48:95–100.
47. Prabhakar AR, Vipin Ahuja, Basappa N. Effect of Curry Leaves, Garlic and Tea Tree Oil on Streptococcus Mutans and Lactobacilli in Children: A Clinical and Microbiological Study. Pesq Bras Odontoped Clin Integr, João Pessoa 2009; 9(3):259-63.
48. MM Fani, J Kohanteb, M Dayaghi. Inhibitory activity of garlic (Allium sativum) extract on multidrug-resistant Streptococcus mutans. JISPPD 2007;25 (4):164-68.
49. Lemar .KM, Passa O, Aon MA. "Allyl alcohol and garlic (Allium sativum) extract produce oxidative stress in Candida albicans". Microbiology 2005; 151(10):3257–65.
50. Sivam GP, Lampe JW, Ulness B, Swanzy SR, Potter JD. Helicobacter pylori in vitro susceptibility to garlic (Allium sativum) extract. Nutr Cancer 1997; 27:118 21.
51. Ross ZM, O'Gara EA, Hill DJ, Sleightholme HV, Maslin DJ. Antimicrobial properties of garlic oil against human enteric bacteria: Evaluation of methodologies and comparisons with garlic oil sulfides and garlic powder. Appl Environ Microbiol 2001; 67:475 80.
52. Tsao SM, Yin MC. In vitro antimicrobial activity of four diallyl sulphides occurring naturally in garlic and Chinese leek oil. J Med Microbiol 2001; 50:646 9.
53. Martin KW, Ernst E. Herbal medicines for treatment of bacterial infections: A review of controlled clinical trials. J Antimicrob Chemother 2003; 51:241 6.
54. Ankri S, Mirelman D. Antimicrobial properties of allicin from garlic.Microbes Infect 1999; 1:125 9.
55. 56. Jain RC. Antitubercular activity of garlic oil. Indian J Pathol Microbiol 1998; 41:131.
56. Fani MM, Kohanteb J, Dayaghi M. Inhibitory activity of garlic (Allium sativum) extract on multidrug resistant Streptococcus mutans. J Indian Soc Pedod Prev Dent 2007; 25:164 8.
57. Rabinkov A, Miron T, Konstantinovski L, Wichek M, Mirelman D, Weiner L. The mode of action of allic: trapping of radicals and interaction with thiol-containing proteins. Biochim Biophys Acta 1998; 1379: 233-44.
58. Ledezma E, Apitz-Castro R. Ajoene the main active compound of garlic(Allium sativum): a new antifungal agent. Rev Iberoam Micol.2006; 23:75-80.
59. Jiang XW, Hu J, Mian FI. A new therapeutic candidate for oral aphthous ulcer: Allicin. Med Hypotheses. 2008; 71:897-9.
60. Schnitzler P, Koch C, Reichling J.Susceptibility of Drug-Resistant Clinical Herpes Simplex Virus Type 1 Strains to Essential Oils of Ginger, Thyme, Hyssop, and Sandalwood Antimicrob Agents Chemother. 2007; 51:1859–62.
61. Mayne ST. Antioxidant nutrients and chronic disease: use of biomarkers of exposure and oxidative stress status in epidemiologic research. J Nutr 2003; 133 (Suppl. 3):933-940.
62. Ziu MM, Giasuddin ASM, Mohammad AR. The effect of garlic oil (allium sativum) on DMBA induced salivary gland tumorigenesis in rat. Journal of Islamic Academy of Sciences 1994; 7:189-192.
63. Hsu S, Singh B, Schuster G. Induction of apoptosis in oral cancer cells: agents and mechanisms for potential therapy and prevention. Oral Oncology 2004; 40: 461–473.
64. Jakszyn P, Agudo A, Ibanez R, Garcia-Closas R, Pera G, Amiano P, et al. Development of a food database of nitrosamines, heterocyclic amines, and polycyclic aromatic hydrocarbons. The Journal of nutrition. 2004; 134:2011–4.
65. Milner JA. Mechanisms by which garlic and allyl sulfur compounds suppress carcinogen bioactivation. Garlic and carcinogenesis. Advances in experimental medicine and biology. 2001; 492: 69–81.
66. Dion ME, Agler M, Milner JA. S-allyl cysteine inhibits nitrosomorpholine formation and bioactivation. Nutrition and cancer. 1997; 28:1–6.
67. Williams DLH. Nitrosation Mechanisms. Adv Phys Org Chem. 1983; 19:381–428.
68. Mei XLJ, Liu XY, Song PJ, Hu JF. The blocking effect of garlic on the formation of N-nitrosoproline in humans. Acta Nutrimenta Sinica. 1989; 11:141–5.
69. Cope K, Seifried H, Seifried R, Milner J, Kris-Etherton P, Harrison EH. A gas chromatography-mass spectrometry method for the quantitation of N-nitrosoproline and N-acetyl-S-allylcysteine in human urine: application to a study of the effects of garlic consumption on nitrosation. Analytical biochemistry. 2009; 394:243–8.
70. Peacehealth.org. [updated 2009 December 23; 2012 May 25].Available from http://www.peacehealth.org/xhtml/content/cam/hn-1289005.html.
71. Dehghani F, Merat A, Panjehshahin MR, Handjani F. Healing effect of garlic extract on warts and corns. Int J Dermatol 2005; 44:612–5.
72. Lemar KM, Turner MP, Lloyd D. Garlic (Allium sativum) as an antiCandida agent: a comparison of the efficacy of fresh garlic and freeze dried extracts.

J Appl Microbiol. 2002; 93:398–405.

73. Davis SR, Penie R, ApitzCastro R. The in vitro susceptibility of Scedosporium prolificans to ajoene, allitridium and a raw extract of garlic (Allium sativum) J Antimicrob Chemother. 2003; 5:1593–1597.
74. Ledezma E, Marcano K, Jorquera A, De Sousa L, Padilla M, Pulgar M, ApitzCastro R. Efficacy of ajoene in the treatment of tinea pedis: a doubleblind and comparative study with terbinafine. J Am Acad Dermatol. 2000; 43:829–832.
75. Reuter HD, Koch HP, Lawson LD. Garlic: The science and therapeutic application of Allium sativum L. and Related Species. In: Koch, HP, LD Lawson, editors. Therapeutic effects and applications of garlic and its preparations. Baltimore: Williams and Wilkins. 1966. p.135–213.
76. Soffar SA, Mokhtar GM. Evaluation of the antiparasitic effect of aqueous garlic (Allium sativum extract in hymenolepiasis nana and giardiasis. J Egypt Soc Parasitol. 1991; 21:497–502.
77. Hogg Jennifer. UK Medicines Information Complementary Medicines Summary, "Garlic Supplements". [Serial on the Internet]. Cited 07-07-2007 Available At http://www.ukmi.nhs.uk/Med_info/ documents/GarlicSupps.
78. Barnes J, Anderson LA, Phillipson JD. Herbal Medicines. 2nd edition. London: Pharmaceutical Press; 2002.
79. WHO Monographs on Selected Medicinal Plants. Geneva: Publications of the World Health Organization can be obtained from WHO press. [Updated 2012 April 24;cited 2012 May 25. Available from http://apps.who.int/medicinedocs/documents/s14213e/s14213e.pdf.
80. True star health.com. Truestar Health & Healthnotes, Inc., [cited 2012 May 25]. Available from http://www.truestarhealth.com/Notes/2093008.html.
81. Lee HJ, Park HS, Kim KH, Kwon TY, Hong SH. Effect of garlic on bacterial biofilm formation on orthodontic wire. Angle Orthod 2011; 81:895 900.
82. Borrelli F, Capasso R, Izzo A. Garlic (Allium sativum L.): Adverse effects and drug interactions in humans. Mol Nutr Food Res 2007; 51(11):1386-97.