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Review Article

GARLIC: NATURE'S PANACEA

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ABSTRACT

Garlic, a very common condiment found in our kitchens has immense therapeutic potential. It has been used since ages in different civilizations and eras for therapy in diverse conditions. However, somewhere down the lane, its health benefits were forgotten with very few researchers doing studies on it and demonstrating its benefits in various disorders of the cardiovascular, respiratory, central, and peripheral nervous systems including dermatological and reproductive disorders. However, with a boom in the Nutraceutical industry in the past few decades, renewed interest has been generated in this age-old remedy with it becoming a very popular health supplement. This review focuses on the health benefits of this wonder food. It also emphasizes the need to find the right therapeutic dose at which it can be therapeutically beneficial and paves the way for future research.

Keywords: Garlic, Antioxidant, Dementia, Lipid lowering.

INTRODUCTION

Garlic is a common household kitchen condiment used very often to add taste to our food. However, what is very interesting to note is that it is one of the earliest plants documented in the literature for its beneficial therapeutic effects [1]. In this review, facts about the garlic plant, its medicinal uses in the bygone eras, present and future implications will be elaborated.

THE USE OF GARLIC IN ANCIENT CIVILISATIONS AND BYGONE TIMES

The ideology of garlic having healing properties might have propped up due to its pungent odor which kept other humans away and thus would also help to keep diseases and other animals away.

The earliest recordings were recovered from the Egyptian civilization where garlic was not only found to be a great part of the diet of the natives, but also of the 875 medicinal preparations contained in the Egyptian book Codex Ebers, 22 of them contained garlic. Garlic was not only fed to the working class and laborers to boost their strength but the use of garlic among the Royal class also came to the limelight when well-preserved garlic cloves were obtained from the tombs of Tutankhamun. The Egyptians also used garlic in embalming and mummifications [2].

Even the Talmud, a Jewish religious text also bears writings where garlic was used for the treatment of parasitic infections, [3] as well as to promote marital relationships.

Garlic dominated the field of health in ancient Greece which was very evident from various instances such as composition of spells found in the Greek magical papyri from the second century, as well as remedies for problems of eyelids in plays by the Greek writer Aristophanes. Garlic was fed to the soldiers before the war to improve their performance in the battlefield. Literature also reveals that athletes were fed garlic just before the event in order to improve their performance in the early Olympics [4]. Hippocrates, the father of medicine also advocated the use of garlic for respiratory complaints [3]. Thus, it is clear that the Greeks no doubt had very early on recognized the potentials of this wonder food.

Ancient Rome was also not spared of the splendor of garlic as it formed a large part of the diet particularly for sailors and soldiers. Dioscorides was a Greek physician, who served Nero's army and was the author of a five volume treatise that postulated that garlic was a blood cleaner. Garlic was also used for treatment of gastrointestinal and joint disorders, seizures, and animal bites. Medical care in Rome was greatly influenced by the writings of Pliny the Elder who wrote an extensive compilation of remedies, the natural history which was first printed in 77 CE and translated several times. This book listed as many as twenty-three uses of garlic for a variety of disorders. Galen, the father of galenic pharmacy named garlic as "rustic's theriac" for its popularity in folk medicine.

Initially used as a preservative, garlic in ancient Chinese medicine was used in combination with other herbs for the treatment of diarrhea, worm infestation, [5] fatigue, insomnia and headache. There has also been recordings of it being used to treat depression and male infertility [6].

Garlic was used extensively for its healing properties in Ancient India with it being mentioned in the Vedas [7]. The ancient systems of medicine especially Ayurveda and Unani also made use of this wonder food with writings in the Charaka Samhita recommending the use of garlic for cardiovascular disorders and arthritis. In ancient Tibet, many recipes to treat stomach disorders which was grown in the gardens of Babylon and was referred to as the "rank rose" [7]. The Ancient Israelis used garlic to stimulate starvation and to kill parasites.

Much of the popularity of garlic in the field of medicine was maintained by the Arab physicians who used it very frequently as remedies for various disorders in the middle ages. During these times in Europe, garlic was predominantly grown in monasteries. The most important document is the Hortulus script where garlic predominantly featured. It was used to treat constipation and to prevent heat stroke in workers [6]. During the later-partof the 12th century, the Abbess of Rupertsberg wrote that eating garlic raw was much better than eating it cooked. In Salerno, garlic was classified as a hot food that generated heat in the winters and limited development of breathing disorders. Garlic also found great use in the Dark periods of Plague [8,9].

The advent of the Renaissance laid importance on medicinal plants with physic gardens being opened in major cities where garlic was one of the most common plants grown. Dr. Pietro Mattioli, a great physician of the 16th century, recommended use of garlic for kidney stones and expelling after birth. The wealthy English also used garlic for toothache, constipation, dropsy, and plague [10].

Moving toward modern times, in 1858, Louis Pasteur noted that garlic killed microbes like bacteria and *Helicobacter pylori* and his

observations were strengthened by the ability of garlic to keep down typhoid, diphtheria and cholera in the 19th century [11]. Lekrek, a French therapist, also used garlic successfully as a prophylactic remedy to control the "Spanish Fever" pandemic in 1918 [12].

Native Americans used garlic not only in tea and also as a stimulant, expectorant and tonic. In 1917 and 1918, people wore garlic necklaces to ward off influenza. In Russia, not only was it an all-time favorite remedy of Russian physicians, garlic was used to treat the wounded soldiers of the Russian army not only in the first world war but also in the second one which was well after the discovery of the world's first antibiotic, penicillin. Thus, garlic was also known as Russian penicillin or natural antibiotic [13].

GARLIC PLANT AND ITS CHEMISTRY

The garlic plant (*Allium sativum*) is a bulbous plant that belongs to the kingdom Plantae, order Asparagales, family Amaryllidaceae, subfamily Alloideae, and genus Allium. There are broadly two subspecies [13] and hundreds of varieties [14] which include *A. sativum* var. *ophioscorodon* (hard necked garlic) and *A. sativum* var. *sativum* (soft-necked garlic). It has been referred to as camphor of the poor, da suan, lasun, nectar of the gods, poor man's treacle, rason, rust treacle, stinking rose in different parts of the world.

The active principle of garlic which was first discovered by Chester Cavallito and team in 1948 is allicin which has been demonstrated to have antimicrobial and antifungal properties [15] (Fig. 1). This compound is not present in garlic naturally but is formed by the cleaving of alliin (along with S-allyl cysteine) by the allinase enzyme which occurs only when a pod of garlic is chopped, crushed or damaged and is responsible for garlics' characteristic pungent odour (Fig. 2). This enzyme is heat unstable [16] and irreversibly deactivated below a ph of 3 and thus allicin is not generated endogenously in the body from the consumption of fresh whole garlic [17,18]. Recent studies have also shown that apart from allicin, many other polar compounds offer health benefits with advantages of them being heat stable and not generating odour [19].

Including allicin, garlic contains 33 sulfur compounds, several enzymes, minerals including calcium, copper, iron, and zinc, vitamins A,B1, and C, flavonoids, and saponins [20]. It is also a factory of essential amino acids [21]. However, in typical servings of 1-3 cloves per day, initially proposed by the German E monograph in 1998,garlic has no significant nutrition value [22] (Table 1). Much debate still arises as to the daily recommended values of garlic.

GARLIC SUPPLEMENTS

The nutraceutical industry has boomed in the past two decades. Herbal supplements for every complaint and sigh of a patient are recommended and it is not surprising that a wonder condiment like garlic was found to used more than twice of other common 91 supplements [23]. The beneficial effects of garlic has been exploited in the form of oils, dehydrated powder, oil macerates, and extracts.

Oil capsules: The essential oil content of garlic cloves is 0.2-0.5% which is obtained by steam distillation of garlic cloves. Vegetable oil is mixed with garlic oil in small quantities in order to mask the pungent smell in capsules available in the market to increase palatability.

Dehydrated powder: Garlic powder is mainly produced as a condiment to flavor food by slicing or crushing, then drying, and pulverizing into powder. How effective is it from the nutritional aspect is still controversial as highlighted in the text above.

Oil Macerate: Originally developed for use as condiments, these are mixtures of whole garlic cloves ground into vegetable oil. This form has a potent garlic odor which is attributed to allicin. Being high in fat, they cannot be consumed on a regular or daily basis.

Extract: The garlic used for extract preparation is grown in selected farms under special organic conditions. Whole or sliced garlic cloves are soaked either in purified water or diluted ethanol in steel tanks for varying amounts of time. The solvent is then concentrated and used. The extract, especially the one that has been aged for as long as up to 20 months and known as aged garlic extract (AGE) contain only water-soluble constituents and a small amount of oil-soluble compounds. These water soluble compounds are mild and more beneficial sulfur-containing, antioxidant rich amino acids such as S-allylcysteine (SAC), S-allylmercaptocysteine, and non sulphur Maillard reaction products. SAC has a 98% absorption rate into the blood-making it have great bioavailability. SAC is the key compound in AGE and is used to standardize it [24,25]. SAC levels can be easily detected in the plasma, liver and kidney after oral intake and is at present the only reliable compliance marker in humans for studies involving garlic supplements [26,27]. It is also worth mentioning that the entire production process in making AGE is subject to 250 stringent quality checks to ensure its safety and efficacy, all of which conforms to international goods manufacturing

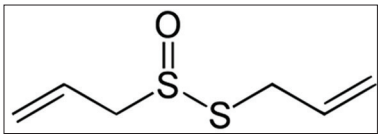

Fig. 1: Allicin - the active principle of garlic

Table 1: Important nutrients in 100 g of garlic

Energy	623 kJ
Carbohydrates	33.06 g
Fat	0.5 g
Protein	6.36 g
Vitamins-Thiamine	0.2 mg
Riboflavin	0.11 mg
Niacin	0.7 mg
Pantothenic acid	0.596 mg
Pyridoxin	1.235 mg
Vitamin C	31.2 mg
Calcium	181 mg
Potassium	401 mg
Magnesium	25 mg
Phosphorous	153 mg
Sodium	17 mg
Iron	1.7 mg
Selenium	14.2 mcg

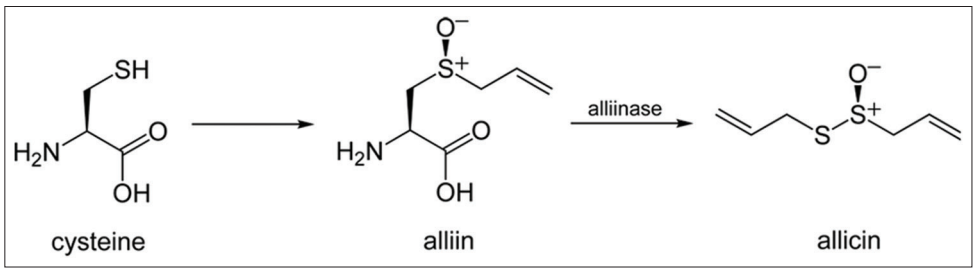

Fig. 2: Formation of allicin from alliin by the alliinase enzyme

practice guidelines [28]. The US National Cancer Institute tested SAC toxicity as compared to other typical garlic compounds and found that SAC is less toxic than allicin and diallyl disulfide (DADS) [29].

HEALTH BENEFITS OF GARLIC

Central nervous system disorders: Research into the pathogenesis of dementia has revealed that there are links between cardiovascular disorders and Alzheimer's dementia [30]. Vascular dementia, which is the second most common dementia after Alzheimer's in the elderly has also been attributed to dyslipidemia [31]. Animal studies have demonstrated that lipid peroxidation may be responsible for the aging process and that intake of hypercholesterolemic diets can result in microglial activation [32] and beta-amyloid plaque deposition [33] and thus can be implicated in pathogenesis of dementias with mixed pathology.

Various animal experiments have revealed that garlic extracts lowered plasma lipid and cholesterol in rats, rabbits, chickens, and swine [34-37] and to possess antithrombotic [38,39] and fibrinolytic properties. These results were also observed in human without history of cardiovascular disease was included and a lowering of low-density lipoprotein-cholesterol [40-43] reduction in platelet aggregation and a stimulation of fibrinolysis has been proved [37,44-47]. Apart from this, garlic has known to be a good antioxidant with remarkable effects on free radical-induced organ damage [26]. The strong antioxidant properties of AGE in particular have been proved to modulate neurobehavioral and neurochemical changes in areas of focal ischemia in a study done by occlusion of the middle cerebral artery of male Wistar rats [48]. Garlic oil has also been demonstrated to have neuroprotective activity in ischemia and reperfusion-induced brain injury. Apart from this, the antioxidant effects of another garlic sulfur compound diallyl tetrasulfide (DTS) has been demonstrated against cadmium [Cd] induced toxicity in the brain [49] and kidneys [50]. These effects have however not been very well-studied in humans and further studies are required.

Antiapoptotic properties have also been attributed to the sulfur compound DADS [51] present in garlic which has been hypothesized to produce neuroprotective effects by activating phosphatidylinositol 3kinase (P13 K) and inactivating glycogen synthase kinase-3 (GSK-3) cytochrome c, caspase - 3 and poly (ADP-ribose) polymerase (PARP). The amelioration of cognitive decline in animal models of Alzheimer's disease (AD) has also been attributed to the antiapoptotic effects of garlic [52].

Thus, with increasing knowledge on the association between cardiovascular risk factors, dementia and AD, the antiatherogenic, antioxidant, and anti-apoptotic effects delivered by garlic may be extended to its neuroprotective action, helping reduce the risk for cerebrovascular disease and dementia. However, more well-designed randomized, larger clinical trials of longer duration using well-standardized preparations of garlic are needed to be conducted to support these effects.

Cardiovascular system disorders: *In-vitro* studies have demonstrated the cholesterol and lipid lowering, antiatherogenic, antithrombotic, antiplatelet effects, antioxidant, and fibrinolytic effects as stated above, which also proves to be beneficial in coronary vessel disease. Garlic extract also has been found to modulate the production and function of nitric oxide in rat pulmonary arteries [53] along with beneficial effects on the heart rate [54] and blood pressure [55]. In human studies, a decrease in blood pressure was observed in patients with essential hypertension [56]. Another study revealed that when garlic was given in injection as 60 mg/day in 10 days to patients with unstable angina symptoms resolved with lowering of blood glucose level in those having hyperglycemia [57]. Chronic garlic powder intake has been found to decrease age-related decrease in aortic stiffness and thus protect the elasticity of the aorta in the elderly [58]. Garlic has also been found to increase blood flow in peripheral tissues, which has been hypothesized to interleukin-6 production [59]. The cardioprotective effects of garlic have been attributed to hydrogen sulfide generation which are generated by conversion of studies where patients with or residual polysulfides by erythrocytes and in turn relax the vascular smooth muscle and causes vasodilation of blood vessels, and thus decrease blood pressure [60]. AGE when consumed over 1-year reduced calcification of coronary vessels in patients taking statins [61].

Garlic as the only therapy for cardiovascular disorders is still not recommended and the supplements should be used only as adjuvants with lip lowering drugs in hypertension [62].

Respiratory disorders: A study showed that subjects who consumed raw garlic two or more times in a week had a 44% decreased risk of developing lung cancer [63]. Garlic has also found to be a wonderful supplement in cold, [64] acute, and chronic respiratory illnesses and have antimicrobial, antifungal, and antiparasitic properties. Ajoene, a sulfur compound present in garlic has been found to interrupt the communication system in Pseudomonas aeruginosa, which is the cause of chronic infections in cystic fibrosis [65]. However, garlic allergen has been demonstrated to be involved in the pathogenesis of occupational asthma in spice mill workers [66].

Gastrointestinal disorders: The efficacy of garlic as an antihelminthic has been proven in animals [67,68]. A pilot study in dyspeptic patients with *H. pylori* showed that 4 mg garlic oil capsules did not inhibit the organisms' growth [69]. In another *in-vitro* study garlic by virtue of suppressing inflammatory cytokine production has found to ameliorate inflammation in inflammatory bowel disease [70]. High intake of raw or cooked garlic has been found to be associated with lower risk of stomach and colorectal cancers [71].

Reproductive system disorders: Researchers believe that garlic acts as a natural contraceptive because it has been found to cause irreversible sperm mobilization and decrease the viability of sperms [72]. However, a higher garlic supplementation over a longer period of time caused an increase in epididymal spermatozoa in adult rats [73]. Garlic has shown to possess controversial effects on testosterone production [74,75]. Cooked garlic has been found to decrease whereas raw garlic has been found to hasten the onset of benign prostatic hypertrophy [76]. Garlic extract has been found to decrease the occurrence of prostate cancer [77].

Endocrine system disorders: Garlic is recognized for its therapeutic potential for controlling diabetes and its subsequent metabolic complications. The hypoglycemic effect of garlic has been attributed to the presence of allicin and the other sulfur compounds. Studies have shown that the oral administration of raw garlic significantly reduces blood glucose levels and improves insulin sensitivity in garlic treated rats. Administration of aqueous garlic in patients with Type 1 diabetes has been reported to increase insulin sensitivity. Furthermore, metabolic complications such as increased serum triglyceride, insulin and uric acid levels usually observed in diabetic rats were normalized after garlic administration [78]. Decreased weight gain has also been attributed to garlic in diabetic rats but on the contrary in a study done in 1-day young cocks revealed that garlic odor stimulated the appetite center and resulted in increased food consumption [79].

Dermatological disorders: AGE protects has been found to protect against free radical and UV-induced skin damage [28]. Garlic powder causes increased capillary skin perfusion by vasodilatation of precapillary arterioles [80]. Topical application of garlic extract has also been proposed to be beneficial in psoriasis, alopecia areata, keloid scars, cutaneous corn, to aid wound healing, to treat viral and fungal infections of the skin, cutaneous leishmaniasis, and as an anti-ageing agent [81].

Infections: The effectiveness of garlic has been highlighted not only against many species of bacteria, but also against viruses, parasites,

protozoans, and fungi [82]. Garlic extract has been found to inhibit both Gram-positive and Gram-negative bacteria like *Staphylococcus*, *Streptococcus*, *Lactobacillus*, *Pseudomonas*, *Shigella*, *Salmonella*, *Proteus* and *H. pylori* [83]. Amongst the fungi, it has been found to inhibit the growth of *Malassezia furfur*, *Candida albicans*, *Aspergillus* and other *Candidal* species with an efficacy equal to that of ketoconazole [84]. Interestingly, garlic has been recommended as an alternative agent for therapy of MRSA [85] and in multidrug-resistant tuberculosis [86].

ADVERSE EFFECTS AND DRUG INTERACTIONS OF GARLIC

The common adverse effects are the pungent smell reflected in the breath and body odor, indigestion, and flatulence noticed after oral administration of garlic cloves. Burns and contact dermatitis are the most adverse effects of topical administration of raw or crushed garlic [87]. Allergic reactions are rare, however, contact dermatitis, rhinoconjunctivitis, asthma, contact dermatitis have been reported [88].

Studies on drug interactions of garlic have yielded controversial results. Initially, studies showed that garlic prolongs the action of anticoagulant drugs and lead to prolonged studies, but this has been disproved in recent studies [89]. It has also been reported that garlic powder induces cytochrome 450 enzymes and decreases the efficacy of protease inhibitors, but this has not been observed with the other formulations [90].

CONCLUSION

Sufficient evidence is now present that garlic is no doubt a wonder food useful as an alternative treatment for various disease conditions. However, before garlic can be considered a safe and effective drug, further research in humans is mandatory as very well-evident most of the studies are *in-vitro* experiments and animal studies. Furthermore, different formulations, raw, and cooked garlic have differential effects. Further studies are also required in order to standardize the content of the active principles in order to determine the most effective dose and dosage form for availing maximal health benefits with minimal side effects. Methods to overcome the pungent smell, which directly affects consumption in patients is required in order to increase palatability. Furthermore, stringent regulations need to be placed on the supplements available in the market in order to ensure quality and safety of the products available.

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