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Original Article

GARLIC: IT'S ROLE IN ORAL AND SYSTEMIC HEALTH

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Abstract:
A range of treatment modalities are available for the treatment of different oral diseases.The frequent use and misuse of currently available therapeutic agents has led to the evolution of increased incidence of adverse effects and development of resistant strains. Hence the search for an alternative option continues. Medicinal plants have been used as traditional treatment agents since ages. Garlic (Allium sativum) has been recognized for a number of therapeutic properties in the traditional system of medicine. Allium sativum is traditionally employed to treat infection, colds, diabetes, heart disease, and a host of other disorders. Clinically, it has been evaluated for lowering blood pressure, cholesterol, and glucose concentration, as well as for the prevention of arteriosclerosis and cancer. It is well known for its potent anti- inflammatory, anti- oxidant, anti-bacterial and antimutagenic properties. This article aims to review the efficacy of garlic in maintaining oral health in particular and overall health in general.

Key words: Garlic, Allium Sativum, P. gingivalis, Cardiovascular diseases.

Introduction :

Oral diseases qualify as major public health problems owing to their high prevalence and incidence in all regions of the world. An adverse oral health condition affects three aspects of daily living: 1) systemic health, 2) quality of life, and 3) economic productivity. Numerous studies have suggested that there is a strong association between oral health and systemic health.[1]In developed countries 10% of public health expenditure is related to curative dental care. Whereas in most developing countries, expenditure to oral health care is very low; limited access to dental healthcare is generally restricted to emergency dental care or pain relief. While there has been a marked improvement in oral health in most developed countries, it is deteriorating in developing countries specially among children from low socio-economic status.[2] With the rise in disease incidence, resistant pathogenic bacteria, opportunistic infections in immune compromised individuals and financial considerations in developing countries there is considerable interest in the development of alternative prevention and treatment options and products for oral diseases.[3, 4]Traditional plants and natural phytochemicals can treat bacterial infections and are considered as good alternatives to synthetic chemicals.[5] Numerous traditional medicinal plants have been evaluated for their potential application in the prevention or treatment of oral diseases. Garlic is one of the most extensively investigated medicinal plants since ancient times. With its high trace mineral content and enzymes, sulfur containing compounds, garlic has shown anti-viral, anti-bacterial, anti-fungal and antioxidant abilities. Garlic extract has been shown to have a wide spectrum inhibitory effect on the growth of various gram-positive and gram-negative bacteria and is also active against multi-drug resistant organisms such as Pseudomonas aeruginosa, Klebsiella pneumonia, and Mycobacterium tuberculosis.[6]

Here, we review the clinically relevant effects of garlic, focusing on potential mechanisms involved in the response to garlic and the potential clinical implications associated

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with its consumption.

Garlic is a perennial plant with white, starry flowers and bulb clusters of individual teardrop shaped cloves encased in dry skin-like papers that unite to create the bulb. The garlic bulb is the part of the plant most often used as flavoring agent and medicinal herb. Garlic can be eaten raw, chopped, minced, or juiced. It has a characteristic pungent, spicy flavor that mellows and sweetens considerably with cooking. Garlic otherwise known as *Allium sativum*, is a species in the onion genus from Liliaceae family. Garlic is grown globally, but China is by far the largest producer of garlic followed by India, South Korea, Spain, and the United States.

Historical Perspective :

For thousands of years, garlic has been used throughout the world as a medicine. Sanskrit records, from approximately 5000 years ago, describe the use of garlic remedies. Chinese, Egyptian, and Greek documents from Hippocrates, Aristotle and Pliny cite numerous therapeutic uses for garlic. In 1844 Theodor Wertheim, a German chemist, distilled a pungent substance from garlic and called it allyl, the Latin name for garlic. Four years later, Louis Pasteur in Paris showed that allyl could inhibit the growth of bacteria. This was a great discovery because 150 years ago, doctors had nothing to eradicate bacteria. The Babylonians, Egyptians, Phoenicians, Vikings, Chinese, Greeks, Romans and Hindus have adopted a number of therapeutic uses for this botanical (Murray 2005).Garlic was used as a remedy for intestinal disorders, flatulence, worms, respiratory infections, skin diseases, wounds, symptoms of aging and many other ailments. Garlic thus acquired a reputation in the folklore; modern science has created a large and fast growing body of scientific research on this medicinal herb.[7]

To date thousands of scientific articles from all over the world have gradually confirmed the traditionally recognized health benefits of garlic. Biological responses of garlic include[7]

- Anti bacterial
- Anti viral
- Anti fungal
- Anti oxidant
- Anti cancer,
- Anti aging effects
- Reduction of risk factors for cardiovascular diseases
- Restoration of physical strength
- Resistance to various stresses
- Stimulation of immune function.

Chemistry of Garlic :

The chemistry of garlic is quite complex and clinical pharmacological properties of garlic have been extensively studied. Whole garlic cloves are intact bulbs that contain an odorless, sulfur-containing amino acid derivative, a covalently bonded compound with the chemical formula $C_6H_{11}NO_3S$(Figure 1). The primary sulfur-containing constituents in whole, intact garlic are the ? glutamyl cysteines and *S* allyl cysteine sulfoxides, including alliin.[7]

When the bulb is crushed or cut, alliin is altered by the enzyme, alliinase and is converted into allicin. Allicin ($C_6H_{10}OS_2$) is an oily, yellow liquid that gives garlic its characteristic odor. (Figure 2)

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 (Fenwick and Hanley 1985) and ajoene (Block et al. 1984). At the same time, ? glutamylcysteines are converted to *S*-allylcysteine (SAC) via a pathway other than the alliin/allicin pathway. SAC contributes heavily to the health benefits of garlic.

Mechanism of action of Garlic :

Broadly the mechanisms of action of garlic in oral health care are: its role as a strong antioxidant, antibacterial, antiseptic and immune - modulatory effect.[7]

Antimicrobial activity of garlic against oral bacteria :

Cavallito and Bailey [8] confirmed that allicin is primarily responsible for the antimicrobial action of garlic. Its main mechanism of action is by blocking thiol-containing enzymes, including cysteine proteases and alcohol

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dehydrogenases.[9, 10] Cysteine proteinase enzymes are among the main culprits in infection, providing infectious organisms with the means to damage and invade tissues. Alcohol dehydrogenase enzymes play a major role in these harmful organisms' metabolism and survival.

The active component of garlic extract, allicin partially inhibits DNA and protein synthesis, and entirely inhibits RNA synthesis.

Garlic extract has shown to have a wide spectrum of antibacterial activity, including effects on, Staphylococcus, Streptococcus, Klebsiella, Escherichia, Salmonella, Proteus, Clostridium, Mycobacterium and Helicobacter species.[9,10]

Groppo FC et al [11] demonstrated that a mouth wash containing garlic extract was more effective at reducing the total salivary bacterial count and the streptococcal mutans count.

Ghannoum MA [12] described marked inhibitory effect of garlic against C. albicans.

Bakri IM [13] reported that garlic extract was slow and less active against oral Gram-positive species when compared to a range of Gram-negative species. This difference between gram negative and gram positive organisms is due to inability of garlic extract to invade the thick peptidoglycan layer in the Gram positive cell envelope.

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.[10]

According to some investigators garlic was effective against antibiotic resistant organisms.[14] On the other hand; some investigators have demonstrated that certain mucoid bacterial strains were discovered to be resistant to allicin. Due to unidentified reasons, it was assumed that penetration of allicin into the bacteria was restrained by hydrophilic capsular or mucoid layers.[15]

Antioxidant effects of Garlic :

Oxidative stress is recognized as one of the pathogenic mechanisms of chronic inflammatory diseases, including cardiovascular disorders and cancer. Consequently, compounds with antioxidant properties may be used to prevent oxidative stress-mediated diseases.[16]

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 S-allycysteine (SAC) and S-allylmercapto-L-cysteine, by displaying radical scavenging activity and modulating cellular antioxidant enzyme activity.

Antioxidant properties of garlic have been demonstrated in animal disease models. Aqueous garlic extract reduces oxidative stress and prevents vascular remodeling by suppressing NAD(P)H-oxidase in the fructose-induced metabolic syndrome model in rats.[17]

SAC also reduces lipid peroxidation and superoxide radical production, and elevates Cu-Zn-superoxide dismutase activity in 1-methyl-4-phenylpyridinium-induced Parkinsonism in mice.[18]

In recent years, numerous human intervention studies have examined the antioxidant influence of garlic in humans. Imai and coworkers[19] studied the antioxidant properties of three garlic preparations and organosulfur compounds and observed that aged garlic extract exhibited radical scavenging activity protecting endothelial cells from injury by oxLDL.

Dhawan V [20] reported reduced oxLDL and 8-iso-prostaglandin F2 alpha levels, accompanied by a significant reduction in both systolic and diastolic blood pressure in hypertensive patients on two months of garlic oil supplementation.

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These results suggest that garlic has potent antioxidant activity in delaying the onset and development of chronic inflammatory diseases, including cardiovascular disorders, diabetes cancer, and neurodegenerative diseases caused by an imbalance between free radical production and antioxidant defenses.

Immunomodulatory Effects :

Sufficient evidences suggest that garlic may have significant enhancing effects on the immune system. Extensive studies are conducted on animals, in vitro and in vivo. However, the human studies that have been conducted are encouraging.

Abdullah TH et al [21] demonstrated positive effects on immunoreactions and increase in the percentage of phagocytosing peripheral granulocytes and monocytes on using an alliin standardised garlic powder preparation. Another human study conducted on AIDS patients with an unrefined garlic extract (5-10 g/day) demonstrated a major increase in the percentage of natural killer cell activity.[21]

Anti-inflammatory :

Agarwal et al [22] demonstrated suppression of the nuclear factor-kappaB activation pathway and inflammatory prostaglandins thus establishing anti-inflammatory activity of garlic.

Therapeutic applications in dentistry :

This potent anti- inflammatory, antioxidant, antibacterial effect and immunomodulatory effect of garlic suggest that it has a therapeutic potential in different oral diseases. Garlic produced a significant reduction in the inflammatory infiltrate and potentially inhibited innate immune response associated with periodontal diseases thus suggesting a therapeutic potential in this chronic inflammatory condition. Garlic can be used as a mouth wash, sub gingival irrigant and as a component in local drug delivery system. It has a great role in the treatment of periodontal diseases.

Other therapeutic applications of garlic :

Antiviral activity :

Many investigators have demonstrated antiviral activity against human cytomegalovirus, influenza virus type 3, vaccine virus, vesicular stomatitis virus and human rhinovirus type 2.[23]

Antifungal activity :

Bakri IM [13] et al confirmed the antifungal activity of garlic against C. albicans described by Ghannoum MA .[12] Ledezma et al [24] demonstrated that ajoene , an active compound in garlic may play a role as a topical fungal agent .

Antimutagenic effects :

Garlic has known to possess anticancer activity because of its various effects on biological pathways. These include free radical scavenging, inhibition of mutagenesis and effects on cell proliferation and tumor growth. Garlic and its organosulphur compounds modulate the activity of several metabolising enzymes that activate (cytochrome P450s) or detoxify (glutathione *S*-transferases) carcinogens and inhibit the formation of DNA adducts in several target tissues. [25] Numerous studies have established the role of garlic in cancer prevention particularly in relation to digestive tract cancers, including esophageal and stomach cancers. [26]

Cardiovascular effects :

Garlic's protective effects on cardiovascular system include:

- Inhibition of hepatic hydroxymethyl glutaryl-CoA reductase activity by alliin and allicin and reduction in LDL-cholesterol. [26]
- Inhibition of platelet aggregation due to suppression of intraplatelet Ca2þ mobilization, an increase in cyclic AMP and cyclic GMP levels, an increase in platelet-derived nitric oxide production, and a reduction in platelet binding to fibrinogen. [28]

Drug interactions :

Few authors have suggested that garlic affects the drug metabolism and alters their pharmacokinetics. It has been hypothesized that garlic organosulfur compounds may be able to prevent glutathione depletion, a compound necessary for liver detoxification. Sabayan et al [29] demonstrated that garlic provides protection against

reactive oxygen species-induced stress on liver function. Sener et al [30] showed that aged garlic can reverse oxidant effects of nicotine toxicity in rats. Maldonado et al [31] showed that aged garlic extract, do not interfere with the antibiotic activity of gentamycin but may improve gentamycin -induced nephrotoxicity. However, as results remain inconsistent and contradictory more well-designed studies are necessary to clarify whether garlic affects the metabolism of drugs and alters their pharmacokinetics.

Adverse effects :

Garlic is generally considered safe but a commonly associated side effect with garlic intake is halitosis, especially when raw forms of the herbs are used. However, Mitchell [32] reported that the odor is decreased when garlic is taken before meals. Odorless garlic formulations are available. However, odorless garlic is often prepared either by adding chemical substances to mask the odor or by cooking the garlic, which may destroy some of the active ingredients. Other side effects include nausea and gastric irritation. Although rare, garlic allergy has been attributed to the protein alliin lyase, which has induced IgE mediated hypersensitivity responses from skin prick testing .[33]

Saw et al [34] warned not to use garlic while on anticoagulant therapy as garlic has been associated with decreased platelet aggregation and bleeding events.

Conclusion :

Over the years, garlic has been a part of tradition, ancient myth, and household remedies. The therapeutic properties of garlic have been known to mankind for ages. Garlic and its compounds have been found to attack multiple targets, which provide the basis for their effectiveness in many different diseases. However, the results observed in human clinical and intervention studies have been inconsistent and the risk of garlic drug interactions is attracting increasing interest. Therefore further experiments are necessary to recognize the definite health benefits and impact of garlic. By looking back into history we can apply some old world uses of garlic for new ways to improve oral and overall health.

Figure 1: Chemical structure of intact garlic

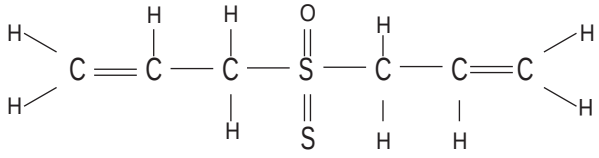
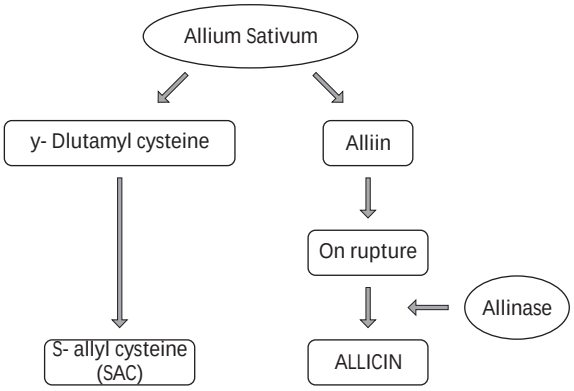


Figure 2: Chemical changes of crushed garlic



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