

Effects of *Allium sativum* (Garlic) and Its Derivatives on Oral Diseases: A Narrative Review

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ARTICLE INFO

Article History

Received: Oct 2020

Accepted: Dec 2020

ePublished: Jan 2021

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ABSTRACT

Garlic is present in the diet of most people around the world. Its use as a medicinal plant has been considered since ancient times and has been mentioned in documents obtained from the Egyptians, Greeks, Indians, and ancient Chinese. Garlic is generally known as a plant with antimicrobial, anti-fungal, anti-thrombotic, analgesic, anti-asthmatic, antipyretic, anti-hypertensive, anti-coagulant, antioxidant, and anti-cancer properties; many of these properties have been proven by scientific research. The present study reviews the original articles published between 2000 and 2020, which investigated the role of garlic and its active ingredients in the treatment of oral diseases. The reviewed studies were often preliminary but their results reveal that garlic has potential therapeutic effects on oral diseases. These studies have provided promising results that advocate the addition of this plant or its compounds to dental health products. However, more detailed clinical and preclinical studies (at cellular and molecular levels) are needed to clarify the mechanism of action of garlic and its active ingredients, such as allicin.

Keywords: *Allium sativum*, Garlic, Oral Health, Oral Disease, Oral Lesion

J Res Dent Maxillofac Sci 2021;6(1):36-44.

Introduction:

Over the last hundred years, the discovery and production of chemical drugs have promoted health around the world; however, herbal medicines are still widely used; 90% of Africans and 70% of Indians use herbal medicines. Adhami et al reported that about 76% of Iranians are familiar with herbal medicines. These medications are also common in developed countries, such as China and the United States. ⁽¹⁻³⁾

Garlic (*Allium sativum* L. Fam. Liliaceae) plays a major role in nutrition and medicine worldwide and is used for disease prevention and treatment in different societies. One of the important characteristics of this plant is that it can be cultivated in most parts

of the world (Table 1). This plant has been used in Egypt, Greece, China, Japan, and ancient India to treat diseases. ⁽⁴⁻⁶⁾ Garlic is an annual herbaceous plant.

The height of this plant reaches 4 feet but varies in different species. The product of garlic is a tuber or bulb that is composed of several small tubers called cloves. Each garlic tuber includes about 12 cloves. This plant is rich in nutrients as 100 grams of garlic contain 61% water, 30% hydrocarbonate, 2% protein, 1% fat, and some amounts of sugar and vitamins A and C. ^(7,8) Garlic is one of the plants recommended in the Quran as a nutrient (Surah of Al-Baqarah, verse 61).

Table 1. Scientific classification of *Allium sativum* L

Kingdom	Plantae
Subkingdom	Viridiplantae - green plants
Supervision	Embryophyta
Order	Asparagales
Family	Amaryllidaceae
Genera	<i>Allium</i> L. - oignon, wild onion, onion
Species	<i>Allium sativum</i> L. - cultivated garlic

Prophet Mohammad (PBUH) said that garlic is a cure for seventy diseases. His statements on the medicinal properties of some plants, such as garlic, have been confirmed by medical research. The accuracy of these statements was proven after fourteen centuries. (9-12)

Various scientific studies have proven the efficacy of garlic in reducing the risk of cardiovascular disease and cancer with its antioxidant and detoxing properties of its active ingredients. For example, phenols and saponins available in garlic have antioxidant properties. Different methods of garlic processing can change its antioxidant activity. Ethyl linoleate in garlic acts as an anti-inflammatory agent by reducing nitric oxide, interleukin (IL)-1, tumor necrosis factor (TNF)-alpha, and prostaglandin E2 (PGE2). The flavonoids in garlic have antiviral properties. Alliin (S-allyl cysteine sulfoxide) is converted to allicin by an enzyme called alliinase. Allicin and other organosulfur compounds of garlic have antibacterial properties. (5,13,14)

Garlic is a source of prebiotic fiber, which makes it useful for dental health and proper digestion. The antifungal and antiviral properties of garlic can help oral health. Oral health refers to the health of teeth, gums, and the entire oral system, which allows us to smile, talk, and eat. Some of the most common diseases that endanger oral health include tooth decay, gum disease, and oral cancer. Also, oral health contributes to general health. For example, periodontal diseases are associated with an increased risk of cardiovascular disease, premature birth, low birth weight, and respiratory diseases. (15) Many oral diseases are preventable. Herbal medicine shows a close association with oral health and treatment

of oral diseases. An example of using plants to maintain oral health is the use of toothbrush wood to brush teeth. (16-20) A review of the related articles indicated no article that summarizes the results of studies conducted on the effects of garlic on oral health. This study summarizes the newly published studies (between 2000 and 2020) on the role of garlic and its active ingredients in oral health. PubMed and Google Scholar databases (from 2000 to 2020) were searched using Medical Subject Headings (MeSH) keywords, i.e. garlic or *Allium sativum* (*A. sativum*), and other keywords, including oral health, periodontal disease, pulp treatment, oral cancer, squamous cell carcinoma, recurrent aphthous stomatitis, herpes, precancerous oral lesions, oral mucosal fibrosis, dry mouth, and pigmented oral lesions. In a search with garlic and oral health keywords, 2,740 articles were displayed in Google Scholar and 14 articles in PubMed. A search in the PubMed database using garlic and oral keywords rendered 443 articles. The relevance of the articles with the research subject was examined by reading their titles and abstracts. Non-relevant and duplicate cases were excluded, and the full texts of 88 research articles on the effects of garlic or its compounds on oral mucosal health were included in the study. In terms of articles with animal and human research, only the results of human research were used. Finally, the results of 30 articles were used to write this review. This information has been presented under separate titles.

Tooth decay:

Tooth decay is an irreversible progressive microbial disease caused by acid production due to bacterial carbohydrate fermentation on teeth. This acid results in hard dental tissue degradation. *Streptococcus mutans* (*S. mutans*) and *S. sobrinus* are the main pathogens involved in the initiation of tooth decay. *Lactobacillus* is a bacterium found in advanced decays. (20-22) Some researchers have reported the positive effects of herbal compounds on the prevention of tooth decay. (23,24) Kshirsagar et al investigated the antibacterial activity of hard- and soft-neck garlic on *S. mutans* and *Lactobacillus acidophilus* (*L. acidophilus*) using the well-diffusion method. The maximum inhibition zone was related to garlic with a hard neck (24 mm) followed by garlic

with a soft neck (18 mm) and chlorhexidine (17 mm).⁽²⁵⁾ Manurung et al obtained the extract of garlic by soaking it in 96% ethanol. They showed a minimum inhibitory concentration (MIC) of 9.39% and a minimum biofilm inhibition concentration (MBIC) of 37.5% against *S. mutans* but no minimum biofilm eradication concentration (MBEC) was observed, indicating that garlic extract could not eradicate *S. mutans* in biofilm.⁽²⁶⁾

Studies conducted by Bin et al, Dewi et al, and Høglund et al revealed that different garlic extracts are effective against *S. mutans* and other cariogenic bacteria.⁽²⁷⁻²⁹⁾ In a clinical study, Agarwal et al evaluated the antibacterial properties of green tea, garlic/lime, and sodium fluoride (NaF) mouthwashes against *S. mutans*, lactobacilli, and *Candida albicans* (*C. albicans*) in children aged 4 to 6 years with severe early childhood caries.⁽³⁰⁾ They observed a sharp decline in the number of *S. mutans* and *Lactobacillus* colonies, but the number of *C. albicans* colonies did not change. They recommended green tea and garlic/lime mouthwashes as a cost-effective alternative to NaF mouthwashes.⁽³⁰⁾ Despite some positive results that support the anticaries properties of garlic extract, Ravi et al published the opposite results.⁽³¹⁾ They examined the antibacterial properties of methanolic extracts of mango twigs, eucalyptus twigs, pudina leaves, and garlic bulbs against *S. mutans*. Eucalyptus and mango twig extracts had many antibacterial properties *in vitro* but garlic and pudina extracts did not show any antibacterial properties.⁽³¹⁾ The differences in the results may be due to the differences in the extraction methods, studied concentrations, and research methods.

Periodontal disease:

Periodontitis is a chronic inflammatory and infectious disease caused by microbial plaque on the teeth and results in the progressive degradation of tooth-supporting tissues, such as gingiva, periodontal ligament (PDL), cementum, and alveolar bone. The most common bacteria involved in chronic periodontitis are *Aggregatibacter actinomycetemcomitans* (*A. actinomycetemcomitans*), *Porphyromonas gingivalis* (*P. gingivalis*), *Bacteroides forsythus*, *Prevotella intermedia*, *Campylobacter rectus*, *Treponema denticola*, and *Fusobacterium tuberculosis*.⁽³²⁾

The most important goal of periodontal treatment is to reduce or eliminate subgingival microorganisms. Due to the emergence of microbial resistance to antibiotics, many efforts have been made to discover new antimicrobial drugs.⁽³³⁾ Given the antibacterial properties of garlic, Shetty et al investigated the effect of ethanol and aqueous extracts of garlic on *P. gingivalis* and *A. actinomycetemcomitans*.⁽³⁴⁾ These extracts showed an antiproteolytic activity on the protease enzyme of *P. gingivalis* and showed inhibition zones of 20 to 25 mm at different concentrations of the extract against this bacterium.⁽³⁴⁾ Aqueous extract of garlic showed higher bacteriostatic activity. *A. actinomycetemcomitans* showed greater resistance against aqueous and ethanol extracts of garlic; The MIC for aqueous extracts of garlic was about 62 µl/ml. They concluded that garlic extracts could have therapeutic effects on periodontitis.⁽³⁴⁾ In a double-blind clinical trial, Zini et al examined the effect of aged garlic extract on periodontitis.⁽³⁵⁾ They randomly assigned 200 patients into case and control groups. Patients were examined at the beginning of the study and 12 and 18 months later. The pocket depth and gingival recession of the patients were measured. The mean pocket depth in the group that used aged garlic extract was 1.06±0.49 mm in the third examination (after 18 months), 1.89±0.74 mm in the first examination, and 1.50±0.46 mm in the control group, indicating the beneficial effects of garlic extract on periodontitis.⁽³⁵⁾

Pulp disease:

Pulpitis or inflammation of dental pulp is the most common disease of the pulp and is mainly caused by a bacterial infection that results in tooth decay. Much damage is imposed on dental pulp in irreversible pulpitis; therefore, removal of pulp or pulpectomy is needed for treatment.⁽³⁶⁾

Sodium hypochlorite (NaOCl) is the preferred chemical substance for root canal treatment as it not only has excellent antibacterial properties but also can dissolve tissue. However, it has disadvantages such as bad taste and odor, tissue toxicity, and weakening the tooth structure. These problems have made scientists focus on the use of herbal medicines to find an alternative to NaOCl.⁽³⁷⁾ Birring et al showed that garlic, similar to 5.25% NaOCl, had antibacterial effects on En-

terococcus faecalis. (38) Siddique et al and Beshr and Abdelrahim found similar results. (39,40) Rao et al compared garlic extract and 2.5% NaOCl solution in terms of human pulp dissolution capacity using the pulp of extracted teeth in vitro. They showed that garlic extract could dissolve the pulp; however, NaOCl is more effective in this regard. (41)

Prabhakaran and Mariswamy also compared the efficacy of 64mg/ml of garlic extract with that of NaOCl in removing the smear layer on 68 extracted premolars and concluded that garlic extract could remove the smear but NaOCl was more effective in this regard. They observed that garlic extract could maintain intertubular dentin integrity. (42) In a double-blind clinical study on children, Kahvand et al compared the clinical and radiographic success of pulpotomy using formocresol and *A. sativum* oil. (43) After pulpotomy, *A. sativum* oil was used in the root pulp of all study groups while formocresol was used only in the formocresol group. The clinical results of patient evaluation three and six months after treatment showed a 100% success rate. The radiographic success rate was similar in all groups (85%). They concluded that *A. sativum* oil could be used for pulpotomy of primary teeth. (43)

Recurrent aphthous stomatitis:

The most common oral mucosal ulcer is recurrent aphthous stomatitis, which affects approximately 5% to 25% of the population. (44)

Allicin (diallyl thiosulfinate) is the main component of fresh garlic. Novianty et al examined the effect of topical allicin in aqueous garlic extract on the re-epithelialization of acetic acid-induced oral ulcers in rats. (45) According to the histopathological results, they concluded that allicin could accelerate wound healing and re-epithelialization. (45) Badr and Al-Mulhim showed the positive effects of aged garlic extract on indomethacin-induced gastric inflammation in an experiment on rats, indicating the anti-inflammatory properties of garlic extract and its usefulness in the treatment of mucosal ulcers. (46) In a study on 36 rats, Anggraeni et al used 20%, 40%, and 80% gels of aqueous garlic extract topically on wounds in the lip mucosa to evaluate the anti-inflammatory properties of these gels twice daily for four days. The valuation of wound diameter

and TNF-alpha level on the fifth day showed that aqueous garlic extract could affect wound diameter and TNF-alpha level. Extracts at 20, 40, and 80% concentrations had effects similar to that of benzydamine in reducing the diameter of oral wounds. The 80% aqueous extract of garlic was more effective than benzydamine in reducing TNF-alpha levels. (47)

Herpes labialis:

The herpes simplex virus type-1 (HSV-1) causes herpes labialis. The virus is usually acquired in early childhood. Infection with this virus is common. Antibodies against this virus can be detected in more than 80% of the population. After the virus enters the body and causes a primary infection, it remains in the trigeminal ganglion and activated occasionally by fever, menstruation, sunlight, and upper respiratory tract infection, leading to the development of herpetic lesions. Acyclovir ointment is usually used to treat this condition. (48) The pharmaceutical industry always tries to find cheaper and more effective drugs with fewer side effects. Garlic has been proven effective against influenza A and B, cytomegalovirus, rhinovirus, human immunodeficiency virus (HIV), viral pneumonia, and rotavirus. In Iran, Razavi et al showed that aqueous and alcoholic extracts of garlic have an inhibitory effect on HSV-1. (49)

Precancerous lesions:

These lesions include erythroplakia, leukoplakia, submucosal fibrosis, Fanconi anemia, and xeroderma pigmentosum. Their removal through surgery is currently the treatment of choice for these lesions but it is associated with a high risk of recurrence. Therefore, non-surgical methods for treating these lesions are highly recommended. Currently, vitamins E and A, carotenoids, folic acid, tea, and cyclooxygenase (COX2) inhibitors are being investigated for this purpose. (50,51) Meshri et al examined the effect of topical S-Allylcysteine, as an anti-cancer agent, for the management of precancerous lesions. (52) S-Allylcysteine is the most abundant organosulfur compound in aged garlic extract. After one month, all patients were satisfied with alleviated pain. The size of the lesion also decreased. Four leukoplakia patients and two lichen planus (LP) patients with

mild to moderate dysplasia showed regression of dysplasia in the histological examination. (52) Abdel-Alim et al examined the effect of aged garlic extract, as a chemopreventive agent, against diethyl nitrosamine (a carcinogenic substance) in rats and found less aggressive malignancies in the group receiving garlic extract. (53) Balasenthil et al indicated that the chemopreventive mechanism of 12-dimethylbenz(a)anthracene (DMBA) in carcinogenesis inhibition is to return RAR β -mRNA expression to normal levels. (54)

Oral submucosal fibrosis:

It is a chronic disease in which collagen is produced increasingly in the epithelium of the oral mucosa, pharynx, and upper esophagus in combination with decreased degeneration, which leads to mucosal fibrosis with reduced elasticity; this results in limited mouth opening and tongue movement. Although there is no definitive treatment for this condition, steroids and nutritional and vitamin supplements are commonly used for this purpose. (49) Jiang et al showed that, if injected intralesionally into subcutaneous fibrosis, allicin in garlic increases mouth opening, reduces the burning sensation in the mouth, and increases the quality of life of patients. (55) Jain et al showed that the use of garlic with pentoxifylline could significantly improve submucosal fibrosis. (56)

Oral candidiasis:

Oral candidiasis is a common opportunistic infection in the oral cavity caused commonly by *C. albicans*. Smoking, dentures, respiratory corticosteroids, reduction in the quantity and quality of saliva, and immunosuppressive diseases and drugs are predisposing factors for oral candidiasis. The clinical manifestations of candidiasis range from the presence of a pseudomembranous layer on the oral mucosa to diffuse redness. The patient may complain of a burning sensation in the mouth. Azoles and polyenes are the most commonly used antifungals and act excellently in controlling oral candidiasis. Garlic also has antifungal activities. (50,57) In a clinical study on 56 patients, Sabitha et al showed that using garlic paste for 14 days, as a clotrimazole solution, is effective in reducing the clinical symptoms of oral candidiasis. (58) In separate laboratory studies, bicans. (59,60)

Mirabadi et al and Haji Fattahi et al proved the effectiveness of garlic essential oil against *C. albicans*. Sreedhar et al also showed that the anti-candida effects of garlic extract are very strong and comparable to that of amphotericin B. (61) Kumar et al observed the inhibitory effects of garlic on *Candida* growth by adding garlic extract to Poly(methyl methacrylate) (PMMA), which is a soft liner in removable prostheses. (62)

Other diseases of the oral cavity:

The search of the literature revealed a lack of studies on the therapeutic effects of garlic or its derivatives on many oral lesions, such as pigmented lesions, human papillomavirus (HPV) lesions, oral lichen planus (OLP), and dry mouth. LP is a chronic cutaneous disease of the squamous epithelium with unknown etiology. This disease can affect skin, nails, scalp, oral mucosa, and genitals. It has a prevalence rate of 0.5% to 2%. OLP is seen more frequently in middle-aged women. (63-65)

Antigen-specific and non-specific mechanisms may be involved in the pathogenesis of this disease. In the antigen-specific mechanism, basal keratinocytes express a specific antigen, which is identified by CD8+ cytotoxic T-cells that kill keratinocytes. However, the non-specific mechanism involves mast cell degranulation and matrix metalloproteinase (MMP) activation in OLP lesions. The combination of these two mechanisms causes T-cells to accumulate in the superficial lamina propria and breakdown the basement membrane. Next, the T-cells migrate into the epithelium; this leads to the apoptosis of keratinocytes. Some studies have indicated that TNF- α , IL-12, IL-2, monocyte chemoattractant protein-1 (MCP-1), and interferon-gamma (IFN- γ) are involved in the pathogenesis of OLP. Considering that garlic or its derivatives can inhibit the transcription of several cytokine genes, such as TNF- α , MCP-1, IL-12, IL-1 β , and IL-6, which are involved in pro-inflammatory responses, it can be concluded that garlic yields positive results in the treatment of OLP. (66)

Conclusion:

Studies on herbal medicines have increased in number during recent decades to replace conventional treatments; oral diseases are no ex-

ception. Various articles have examined the effect of garlic or its derivatives on various oral diseases ^(16,17,24,25,27-30,34,35,38-40,67). The results of these studies have been positive and promising (Table 2).

Garlic and its compounds have been shown to have therapeutic effects on various oral diseases and are effective against cariogenic bacteria, including *S. mutans*, *Lactobacillus*, *P. gingivalis*, and *actinomycetemcomitans*.

Table 2: Effects of *Allium sativum* L on common oral diseases (clinical trial studies)

Disease type	Experimental model	Treatment effects	Reference
Dental caries	Comparison of the antibacterial effects of green tea, garlic with lime, and sodium fluoride (NaF) mouth rinses on <i>Streptococcus mutans</i> , <i>Lactobacilli</i> , and <i>Candida albicans</i> in 45 children with severe early childhood caries	Green tea and garlic with lime mouth rinse can be an economical alternative to NaF mouth rinse for prevention and therapeutics	31
Periodontal disease	Assess the long-term efficacy of aged garlic extract to improve periodontitis in 200 patients	Aged garlic extract is an effective supplement for preventing or improving periodontal disease	41
Pulp disease	Clinical and radiographic evaluation of <i>Allium sativum</i> oil (garlic oil) in comparison with formocresol in primary molar pulpotomy	<i>Allium sativum</i> oil can be used in pulpotomy of primary molars.	49
Premalignant disease	Efficacy of garlic in conjunction with pentoxifylline in the management of oral submucous fibrosis	Choice of pentoxifylline along with garlic is beneficial, affordable, available, and most importantly, a non-invasive treatment modality for oral submucous fibrosis	62

A study indicated that garlic/lime mouthwash could prevent dental caries as much as NaF mouthwash does.⁽³⁰⁾ Another clinical research showed the effectiveness of garlic in reducing the depth of periodontal pockets.⁽³⁵⁾ Garlic extract also has anti-candida, antiviral, and anti-inflammatory properties.^(41,47,49,58) Such promising results advocate the addition of garlic or its derivatives to dental health products. However, the number of articles in this area is limited, and most studies have been conducted on animals. Thus, clinical studies on humans are needed as this plant has few side effects with a high tolerance.^(5,68) The analgesic properties of garlic in the oral cavity have not been investigated.⁽⁶⁹⁾

It can be a good basis for producing a natural analgesic for toothache. Another characteristic of garlic that has not been used in dentistry is its immunomodulatory property,⁽⁶⁶⁾

which suggests garlic as an appropriate drug for oral diseases caused by immunosuppression (such as OLP). Also, more clinical and preclinical studies (at cellular and molecular levels) are needed to examine the mechanism of action of garlic and its compounds, especially allicin. In general, only preliminary studies have examined the role of garlic and its active compounds in the treatment of oral diseases; nonetheless, even these studies have shown that garlic can treat oral diseases.

Acknowledgments:

The authors gratefully acknowledge the financial support of this work by Ahvaz Jundishapur University of Medical Sciences.

sativa and its active constituent thymoquinone in oral health. *Saudi Med J.* 2016;37(3):235-244.

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Cite this paper as: Shooriabi M. Effects of *Allium sativum* (Garlic) and Its Derivatives on Oral Diseases: A Narrative Review. *J Res Dent Maxillofac Sci*. 2021;6(1):36-44.