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Review Article

Natural and Biological Compounds as a Solution to Control and Prevention of Dental Caries

Azam Aliasghari Veshareh[1], Mohammad Rabbani Korasgani [*2]

[1] Department of Microbiology, Faculty of Biological Sciences, Alzahra University, Tehran, Iran

[2] Department of Cell and Molecular Biology & Microbiology, Faculty of Biological Science & Technology, University of Isfahan, Isfahan, Islamic Republic of IRAN

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Abstract

Dental caries, the most common human infection, is a multifactorial disease that cost millions of dollars annually in control and treatment efforts. In recent decades, natural products have gained significant attention for the prevention, control, and treatment of dental caries. This shift is driven by factors such as the increasing resistance of bacteria to antibiotics, the high costs, and several adverse effects associated with some chemical agents. Natural products, derived from l sources like plants, animals, and microorganisms, have demonstrated therapeutic effects, particularly, in controlling dental caries. This review elucidates studies on the impact of antibacterials from various natural products against bacteria causing dental caries. Reliable databases such as Scopus, Science Direct, and Web of Science, were utilized to compile this article. According to the favorable results of these studies, it will be promising to substitute these natural compounds with chemical drugs to prevent and control dental caries in the future.

Keywords: Antimicrobial activity, Biofilms, Herbal extracts, Mutants streptococci, Natural Sources

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Corresponding author: Mohammad Rabbani Korasgani **Email**: m.rabbani@ biol.ui.ac.ir

Introduction

Dental caries is a chronic disease that is prevalent around the world, and people are always susceptible to this infectious disease (1). World Health Organization (WHO) reports show that dental caries is an important health problem affecting 60–90% of schoolchildren and most adults (2). Although there are many prophylactic methods, dental caries is one disease persistent in humans (3). Teeth can be destroyed if proper care is not provided (4). The microbiome of the humans in the oral cavity is composed of various bacteria, fungi, and viruses (3). Microbial pathogens in oral, especially cariogenic bacteria such as *Streptococcus mutans*, are mostly factors in the occurrence of dental caries (5). *Streptococcus mutans* expressing collagen-binding protein can invade human umbilical vein endothelial cells and lead to infective endocarditis (6). Biofilm formation by oral bacteria that are causative resistant to the antimicrobial drug can contribute the development of dental caries (7).

Natural products are generally safe and effective in the control and prevention of many infections and diseases, and the antimicrobial ability of some of these has been assessed against oral cariogenic bacteria (8).

Plant extracts, probiotics, bacteriophages, and other natural products, such as honey and chitosan, can be promising new compounds for the control and prevention of microorganisms related to dental caries. This paper reviews research on the anti-cariogenic effect of these natural products.

Plant extract

Since ancient times, herbal medicine has been used to treat a wide range of diseases, especially infectious diseases. Today, the global approach is toward replacing chemical drugs with herbal alternatives (9). The antimicrobial and antioxidant properties of natural compounds derived from plants have shown the ability to control tooth decay and are promising for maintaining oral and dental health (10).

Plant extract can be useful in removing dental biofilm. For example, studies on Rosa damascena showed that the its extract impacts favorable effects on the growth and inhibition of biofilm formation of *S.mutans* (11). Several studies have observed that Green tea demonstrated inhibitory effects on the attachment and biofilm formation of *S.mutans* (7). A research study in 2021 found that epigallocatechin gallate (EGCG), derived from green tea, can inhibit the growth rate and acid production of *S. mutans* while also increasing the aggregation of Streptococci in the cell suspension (12).

Herbal extracts such as Salvadora persica (13, 14), Mango, Capsicum annuum, Solatnum melongena L. (15), Pomegranate, aloe vera (16), Scrophularia striata (17), are other herbal extracts have been evaluated in various studies for their effects against cariogenic bacteria. . Also, the extraction of essential oils (Eos) from aromatic plants has demonstrated favorable effects on microorganisms causing dental caries. Menthol and eugenol are outstanding compounds that exhibit antibacterial potential effects (18).

Table 1; Some herbal extract against pathogens cause's dental caries.

Extract herbal	Microorganism	Result	References
Mango	*S. mutans*	Zone of inhibition (mm): 13.5	(19)
Eucalyptus	*S.mutans*	Zone of inhibition (mm): 9.5	(19)
Capsicum annuum	*S. mutans*, *S. sobrinus, S.sanguis*	MIC= 250 mg/ml MIC= 125 mg/ml	(15)
eggplant skin *(Solatnum melongena L)* eggplant cap	*S. mutans*, *S. sobrinus* and *S. sanguis* *S. mutans, S. sobrinus* *S.sanguis*	MIC= 250 mg/ml MIC= 125 mg/ml MIC= 500 mg/ml MIC= 125 mg/ml	(15)
Saliva officinalis	*S. mutans* *Lactobacillus rhamnosus* *Actinomyces viscosus*	MIC= 6.25 µg/ ml MBC= 50 µg/ ml MIC= 1.56 µg/ ml MBC= 12.5 µg/ ml MIC= 12.5 µg/ ml MBC= 12.5 µg/ ml	(20)
Pimpinella anisum	*S. mutans* *Lactobacillus rhamnosus* *Actinomyces viscosus*	MIC= 12.5 µg/ ml MBC= 200 µg/ ml MIC= 12.5 µg/ ml MBC= 12.5 µg/ ml MIC= 50 µg/ ml MBC= 100 µg/ ml	(20)
Cinnamomum zeylanicum bark (aceton)	*S. mutans* *Staphylococcus aureus* *Candida albicans* *Saccharomyces cerevisiae*	MIC = - Zone of inhibition (mm): 12.31 MIC = 25 mg/ml. Zone of inhibition (mm): 16 MIC = 12.5 mg/ml. Zone of inhibition (mm): 29.30 MIC = 16.65 mg/ml. Zone of inhibition (mm): 50	(21)
Iranian green tea *Iranian black tea (methanolic extract)*	*S. mutans*	MIC = 150 mg/ml. Zone of inhibition (mm): 9.5 MIC = 50 mg/ml. Zone of inhibition (mm): 10.9	(22)
Pomegranate *aloe vera*	*S. mutans*	Zone of inhibition (mm): 15.33 Zone of inhibition (mm): 0.833	(16)

Rosa damascena	*S. mutans*	MIC= 7.5, MBC=15 Biofilm Rediction =93.93%	(23)
	S. sobrinus	MIC= 7.5, MBC=7.5 Biofilm Rediction =74.90%	
	Streptococcus salivarius	MIC= 15, MBC=15 Biofilm Rediction =84.59%	
	Streptococcus sanguis	MIC= 15, MBC=30 Biofilm Rediction =79.09% (mg/ml)	
Rose water	*S. mutans* *S. sobrinus*	Biofilm Rediction= 80%, 56% Biofilm Rediction=57%, 60%	(24)
Rosa damascena	*S. mutans*	Zone of inhibition (mm): Ethanolic ; 100 µl= 15 200 µl=20.66 , 300µ=23 Methanolic; 100 µl=18 200 µl= 23.66 300µ =25	(25)
Honey	*S. mutans* *S. sobrinus*	Biofilm Rediction =66.43% Biofilm Rediction =33.12%	(26)
Ginger *(Zingiber officinale)*	*S. mutans*	Zone of inhibition (mm): 20	(27)
Streblus asper *Cymbopogon citratus* *Syzygium aromaticum*	*S. mutans*	Zone of inhibition (mm)= 7.3 Zone of inhibition (mm)= 6.5 Zone of inhibition (mm)= 14.4	(28)

Several studies have investigated the effectiveness of chitosan in different formulations, such as toothpaste, mouthwash, and chewing gum. One study showed that toothpaste containing chitosan reduces the number of *S. mutans* in children, with greater effectiveness observed as the chitosan concentration increases (35). Toothpaste formulations containing chitosan combined with other natural materials have been investigated. For example, toothpaste containing chitosan and biosurfactants derived from microorganisms inhibited viability of *S. mutans* in biofilms, can be a suitable substitute for chemical and commercial toothpaste (36).

Another study showed that chitosan mouthwash reduced the count of *Streptococcus spp*, *Enterococcus spp.*, and microbial biofilm formation, compared to commercial mouthwashes (37). Also, one investigation showed that using chitosan chewing gum reduced *S. mutans* numbers by five-fold and decreased *S. mutans* colonies, as well as a minor increase in salivary pH (38).

Honey

Honey bees produce honey by using the nectar of flowers (39). The antibacterial effects of honey were first recognized in 1892, with the primary cause identified as the osmotic effect of the sugars in honey (40). Due to its numerous nutritional and healing

abilities, honey has significant potential for use in the prevention and treatment of oral and dental diseases. In addition, it possesses various biological properties, i.e., anti-inflammatory, antioxidant, anti-cancer and antiseptic effects (41).

Natural honey is useful for different problems in the mouth, such as dental caries, gingivitis, and halitosis (39). Studies have shown that honey can decrease biofilm formation by more than 66% and 33% in *S. mutans* and *Streptococcus sobrinus* respectively (26). A study investigating the effect of honey on oral *Streptococci* revealed that Brazilian honey exhibits antibacterial and anti-biofilm activity (42).

Atwa et al stated that chewing honey reduces the number of bacteria on dental plaque significantly (43). The study showed that honey mouthwashes do not have adverse effects or cause staining of the teeth. These mouthwashes do not contain ingredients including alcohol, artificial color, and sweetener, and therefore do not contribute to halitosis (44).

Manuka honey (40, 45, 46), Honey (47-49) have inhibitory effects on plaque and biofilm formation, as well as on growth reduction of oral bacteria such as *S. mutans*, *Lactobacillus* species.

Probiotics

The World Health Organization (WHO) defines probiotics as live microorganisms that, when consumed in sufficient amounts, provide a health benefit to the host (50). The study and use of probiotics and prebiotics have gained widespread due to favorable effects on health (51). Probiotics have proven helpful in preventing oral diseases, including dental caries and periodontal disease by competing with pathogenic bacteria growth (52, 53). One mechanism that probiotics can cause in inhibiting biofilm formation is biosurfactant production (54).

Several studies have reported the use of probiotic strains to prevent oral diseases, including caries. Probiotics are administered to maintain or restore the natural saprophytic micro-flora against a pathogen invasion, which is central to the development of major oral diseases containing caries and periodontal disease (55). Tablets, chewing tablets, mouthwashes, capsules, and supplements of dietary are different forms of presentation of probiotics (55, 56). *Lactobacillus*, *Bifidobacterium*, *Enterococcus*, *Saccharomyces* (53), *Streptococcus thermophiles*, *Streptococcus salivarius* (57), *Streptococcus oligofermentans* (58) are well known strains used as oral probiotics. In vitro and in vivo studies have shown that probiotics reduce *S. mutans'* colony counts in both adults (59) and children (60).

Selvarajan *et al.* reported that probiotic curd can reduce colony counts of *S. mutans*, *Bifidobacterium dentium*, and decrease pH above the critical level in children's saliva (61).

In a study investigated the effect of vital and supernatant of two probiotics (*Lactobacillus reuteri* and *Streptococcus oligofermentans*) on cariogenic biofilms, it was found that viable probiotics reduce the mineral loss, decrease bacterial numbers , and reduce complex cariogenic biofilms (58).

Bacteriophage

For the first time, Twort and D'Herelle identified bacteriophages as lysing bacterial cells in 1917 (62). Bacteriophages are self-replicating and generally target a narrow range of bacterial strains within the same

species (3)Phage therapy involves the use of bacterial virus or their products to treat or prevent bacterial infection. Lytic bacteriophages can control the oral microflora by lysing sensitive cells and have the potential as specific agents for treating tooth decay (62, 63).

Much of the research pertaining to phage therapy in the oral cavity is still in the preliminary stages. Phages that are active against *Aggregatibacter actinomycet emcomitans, Fusobacterium nucleatum*, and several *Streptococcus* species have been identified. Ideally, active phages against *Streptococcus mutans* could be used to decrease dental caries, but this has not been put into actual practice yet (64).

There are several researches on the isolation of lytic bacteriophages of oral *Streptococci* from different sources such as dental plaque, water, and human saliva (3, 63, 65, 66). In a study, lytic bacteriophages of *S. salivarius* were identified from the Caspian sea, showed that these bacteriophages could potentially significantly prevent dental plaque formation (63).

Bacteriophages can be used in different formulations (mouthwash, chewing gum, toothpaste) for the control, prevention, and treatment of dental caries and dental plaque in modern medicine. Therefore, phage therapy could offer a promising approach for controlling cariogenic bacteria.

Conclusion

Plant extracts, probiotics, bacteriophages, and other products can be promising for preventing and controlling dental caries. Natural products can serve as alternatives for conventional drugs without associated side effects. Additionally, they can be used as adjacent or additive to the use of the present material. However, more research is needed to assess the efficacy and safety of these natural compounds. For people all around the world, natural products are available and can be helpful in controlling dental caries. Many researchers have assessed the effects of natural products on the control of dental caries. We tried to make a short review of recent scientific studies about herbal medicine, probiotics, chitosan, honey, and bacteriophages in the prevention of dental caries that may help increase research in this field and find new natural compounds to control and treatment of this disease.

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