

# Beneficial effects of specific natural substances on oral health

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## ABSTRACT

المواد التي تستهلك يومياً أو أحياناً قد تؤثر على صحة الفم. بعض المواد، مثل الكحول والتبغ وجوز الأريكا، تؤثر سلباً على منطقة الفم. ومع ذلك، فإن بعض المواد الأخرى، مثل العسل والشاي الأخضر، والتي لها خصائص مضادة للميكروبات، والتوت، والتي لها إمكانات مضادة للسرطان، تظهر آثار مفيدة على صحة الفم. فعالية العقاقير الإصطناعية في الحفاظ على صحة الفم لا يمكن تجاهلها؛ يبدو أن فوائد العقاقير الإصطناعية ترتبط بالآثار الضارة والتكاليف العالية. على النقيض من ذلك، يرتبط الاستخدام الطبي للمواد الطبيعية مع السلامة، والقدرة على تحمل التكاليف، والفوائد على المدى الطويل. في هذه الورقة، نستعرض مختلف المواد الطبيعية التي يمكن أن تكون مفيدة لصحة الفم.

Substances that are consumed daily or occasionally may influence an individual's oral health. Some substances, such as alcohol, tobacco, and areca nut, adversely affect the oral region. However, some other substances, such as honey and green tea, which have antimicrobial properties, and berries, which have anticarcinogenic potential, exhibit beneficial effects on oral health. The effectiveness of synthetic drugs in maintaining oral health cannot be ignored; however, the benefits of synthetic drugs are associated with adverse effects and high costs. By contrast, the medicinal use of natural substances is associated with safety, affordability, and long-term benefits. In this paper, we review various natural substances that are potentially beneficial to oral health.

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Various medications are commonly used for managing oral diseases and infections. These substances are mostly chemical and synthetic derivatives, and their users experience several adverse effects. However, we commonly use natural substances that have potential beneficial effects on oral health. In addition to improving oral hygiene, these natural substances have been reported to effectively alleviate various oral maladies. The primary advantage of using natural substances is that unlike their synthetic and chemical counterparts, they do not cause any major side effects.<sup>1</sup> Conventionally, review articles have emphasized the beneficial effects of a single substance on oral health. This paper is unique because it collectively focuses on the beneficial effects of a group of natural substances on oral health, and some of these substances, such as tea, honey, berries, and olive oil, are routinely used and readily available. This review elaborates the beneficial effects of specific natural substances on oral health.

**Tea.** Tea is an aqueous infusion of the leaves of *Camellia sinensis*. It is the most extensively consumed beverage after water. Depending on the technique employed for processing the leaves, tea can be categorized into 3 main types: oxidized black tea, semioxidized oolong tea, and nonoxidized green tea. Tea contains numerous chemical compounds, such as amino acids, carbohydrates, protein, caffeine, catechins, polyphenols, fluoride, and other unspecified compounds. Tea drinkers can benefit from the antioxidants and phytochemicals, such as vitamin C, carotenoids, tocopherols, polyphenols, and flavonoids, present in tea. These components protect against various diseases and oxidative damage. Dental diseases, such as dental caries, gingivitis, and periodontitis, which cause tooth mobility and eventually tooth loss, may adversely affect the general health of an individual. Polyphenols from green tea have been reported to be effective against the cariogenic bacterium *Streptococcus mutans* (*S. mutans*) in humans and experimental animals. Another caries-producing microorganism, *Streptococcus sobrinus* (*S. sobrinus*), was reported to be susceptible to the bacteriostatic activity of oolong tea extract. The antibacterial activity of the



extract significantly reduced caries scores in tea drinkers. Green tea exhibits a strong anticaries effect because the supplementation of drinking water with 0.1% green tea polyphenols measurably minimized pit and fissure carious lesions in rats.<sup>2,3</sup> A study on the effects of a green tea-based mouthwash revealed a considerable reduction in the salivary counts of *S. mutans* and *Lactobacillus spp.* when the mouthwash was used thrice daily for a week.<sup>4</sup>

Supplementation of water supply and dental products with fluoride is the preferred measure for caries prevention. However, in areas lacking fluoridation facilities, similar dental protection can be derived from fluoride present in tea. The antiabrasive and antierosive effects on dentin after rinsing the mouth with a green tea extract (0.61%) were comparable to those observed after rinsing with a fluoride extract (250 ppm) or chlorhexidine extract (0.06%). The fluoride content of black tea is 5 times higher than that of green tea.<sup>2,4</sup> The anticaries effect of tea becomes notable if tea is consumed without sugar. In Japan, an in situ experiment was performed in which a chewing gum containing green tea extract was used as the source of fluoride. The results revealed that the extract increased acid resistance and induced superior remineralization in demineralized enamel lesions.<sup>5</sup>

Chemoprevention is a strategy involving the use of natural or synthetic substances to inhibit the development of cancer, metastasis, and progression of premalignancies to malignancies. Green tea has been demonstrated to be an effective chemopreventive agent against head and neck cancers, including cancers of the oral cavity and pharynx. A study examining cell viability and DNA synthesis in squamous cell carcinoma (OSCC) cells treated with green tea components revealed that the extracts exerted cytotoxic effects on cancerous cells. Moreover, suppression of DNA replication was reported in OSCC cells during posttherapeutic evaluation. Polyphenols in tea, such as theaflavins and catechins, have been found to be highly effective in preventing oral cancer.<sup>5,6</sup>

Epigallocatechin-3-gallate (EGCG) is the most effective chemoprotective polyphenol in green tea. Epigallocatechin-3-gallate constitutes approximately

80% of the total catechins in green tea, and a single cup of green tea contains approximately 300 mg of EGCG. The EGCG levels after the intake of a cup of green tea were reported to be higher in the saliva than in the blood, thus providing additional evidence of the role of tea in preventing oral cancers associated with tobacco use.<sup>7</sup> Additionally, polyphenols in green tea have been reported to facilitate the elimination of halitosis through modification of foul-smelling sulfur compounds.<sup>4</sup> Hence, tea polyphenols are used in products such as chewing gum and mouth sprays, which are used for eliminating bad breath.<sup>8</sup>

**Licorice.** Licorice is the root of *Glycyrrhiza spp.* Studies have revealed that licorice and its bioactive constituents are highly effective in treating common oral and dental diseases such as oral candidiasis, recurrent aphthous ulceration, caries, and periodontitis (Table 1). Glycyrrhizin, a sweet-tasting bioactive ingredient present in licorice, has been reported to exhibit anticariogenic properties. This ingredient has been reported to inhibit the synthesis of insoluble glucans required for biofilm formation by interfering with glucosyltransferase activity of the cariogenic bacterium *S. mutans*.<sup>9</sup> Moreover, adding glycyrrhizin to a phosphate-fluoride solution resulted in the increased uptake of fluoride and facilitated its deposition in the porosities of the demineralized enamel. However, this anticariogenic property of glycyrrhizin was dose-dependent and required a sufficiently long exposure time.<sup>10</sup> Although glycyrrhizin has been demonstrated to exhibit anticariogenic properties, additional randomized controlled studies are required to consolidate these findings. The use of licorice-based lollipops twice daily significantly reduced the salivary counts of *S. mutans* in children. Such products may be attractive anticaries products, particularly for individuals who are susceptible to caries development.<sup>11</sup> Saliva inherently possesses several tooth-defensive properties, including the cleansing effect, buffering capacity, antimicrobial activity, and remineralization activity. Licorice stimulates salivation because of its sweet taste and provides protection against dental caries.<sup>12</sup> Because of the effects of its bioactive constituents, licorice was reported to act as a source of phytochemicals with potential therapeutic effects on periodontal diseases such as gingivitis and periodontitis. Licorice has been demonstrated to directly inhibit periodontopathogens (mainly *Porphyromonas gingivalis*) in addition to affecting the host inflammatory response involved in periodontal diseases.<sup>13</sup> Macrophages pretreated with licorice released significantly less proinflammatory cytokines (interleukin [IL]-1b, IL-6, IL-8, and

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**Table 1** - Beneficial effects of natural substances on oral health

Substance	Beneficial effects and References
Tea	Anticariogenic effect <sup>2-4</sup> Chemoprevention against oral cancers <sup>5-7</sup> Prevention against oral malodor <sup>4,8</sup>
Licorice	Anticariogenic effect <sup>9,11,12</sup> Prevention against gingivitis and periodontitis <sup>13,14,16</sup> Prevention against oral candidiasis <sup>17</sup> In recurrent aphthous ulceration <sup>19,20</sup>
Honey	Use as dressing for infected maxillofacial wounds <sup>25</sup> Minimization of severity of oral mucositis in patients undergoing radiotherapy and chemotherapy <sup>21,26,27</sup>
Propolis	Use as a fixative of oral tissue specimens for biopsy <sup>29</sup> Assistance in normal healing of postoperative oral wounds <sup>36</sup> Superior oral hygiene maintenance in patients with dental implants <sup>40</sup>
Berries	Antiplatelet effect <sup>45</sup> Inhibition of the survival of <i>S. mutans</i> by interference with microbial F-ATPase activity <sup>48,49</sup> Treatment of oral lichen planus <sup>50</sup> Suppression of oral squamous cell carcinoma in oral epithelial dysplasias <sup>51,52</sup>

TNF- $\alpha$ )<sup>14</sup> than the controls on stimulation with *P. gingivalis* or *Aggregatibacter actinomycetemcomitans* lipopolysaccharides. Destruction of the alveolar bone is a characteristic feature of periodontitis. Resorption of the alveolar bone depends on the induction and maturation of osteoclasts. On activation, resorptive osteoclasts adhere to the surface of the bone and cause the dissolution of the mineral and organic constituents of the bone matrix. Glabridin, a phytochemical derived from licorice, has been found to promote bone formation through stimulation of the osteoblasts (bone forming cells) in periodontitis.<sup>12,15</sup> In an in vitro study, an ethanolic extract of licorice (67%) exhibited potent antimicrobial activity against periodontal pathogens at 24, 48, and 72 hours (zones of inhibition [ZOIs] = 10.6  $\pm$  0.5, 10.6  $\pm$  0.89, and 8.6  $\pm$  2.40 mm, respectively). This antimicrobial effect of licorice was comparable with that of the standard antibiotic vancomycin (10  $\mu$ g) (ZOIs = 11.6  $\pm$  1.14, 11.6  $\pm$  1.51, and 10.0  $\pm$  2.54 mm at 24, 48, and 72 hours, respectively).<sup>16</sup> Oral candidiasis is an opportunistic fungal infection affecting the oral cavity. It is caused by excessive growth of *Candida albicans*. The most common clinical forms of oral candidiasis are *Pseudomembranous candidiasis* and *Erythematous candidiasis*. *Pseudomembranous candidiasis* is clinically manifested as creamy-white flecks on the oral mucosa. These pseudomembranous flecks are composed of cellular debris and fungal hyphae. *Pseudomembranous candidiasis* is commonly known as thrush. *Erythematous candidiasis* is usually manifested in wearers of maxillary complete dentures as red and inflamed palatal mucosa beneath the denture. This specific condition is clinically

known as denture stomatitis.<sup>12</sup> Licochalcone A and glabridin, isoflavonoids from licorice, exhibited a potent fungicidal action on *C. albicans*. Both these compounds inhibited *C. albicans* growth, and the minimal inhibitory concentrations were in the range of 6.25-12.5  $\mu$ g/mL. They were also shown to act synergistically with nystatin against oral fungal infections.<sup>17</sup> Recurrent aphthous ulceration is one of the most common and painful conditions of the oral mucosa affecting children and adults. This clinical manifestation of this condition is multiple recurrent small round ulcers.<sup>18</sup> The use of a mouthwash containing deglycerinized licorice extract for 2 weeks alleviated pain and expedited the healing of aphthous ulcers.<sup>19</sup> In a randomized, double-blind clinical trial, using a dissolvable oral patch containing licorice extract for 8 days considerably reduced the size and soreness of aphthous ulcers.<sup>20</sup> For arriving at a conclusion regarding the beneficial effects of licorice in oral diseases, additional clinical studies on oral licorice extract-containing hygiene products such as toothpastes, mouthwashes, chewing gums, and gels are needed.

**Beehive products.** Various products derived from the beehive, such as honey, propolis, and royal jelly (RJ), are medicinally beneficial to humans. Honey is a complex by-product of floral nectar. After collection by worker bees, the floral nectar becomes concentrated because of the evaporation of water within the digestive tract of bees. Honey is composed of sugars (glucose and fructose), vitamins, protein, fatty acids, trace minerals, and enzymes.<sup>21</sup> Propolis is a resinous substance that is derived from plant resins, and it is enriched with the salivary enzymes of bees. It is also known as bee glue.

The constituents of propolis include polyphenols, waxes, aromatic acids, and volatile oils.<sup>21,22</sup> Royal jelly is a substance that is produced by the hypopharyngeal and mandibular glands of worker bees. Royal jelly is used for meeting the nutritional demands of the queen bee and larvae because it is rich in proteins, fats, carbohydrates, and vitamins.<sup>23</sup>

**Honey.** Since ancient times, honey has been a valuable agent for wound dressing. The current research has helped to rediscover the wound healing potential of honey. The efficacy of honey in the healing various types of wounds, including acute, chronic, and infected wounds, has been substantiated. It promotes rapid epithelialization and vascularization of the wound. Moreover, the wound healing is expedited because of the antimicrobial and immune-modulatory effects of honey. The efficacy of honey as an antibacterial agent has been reported to be considerably higher than that of standard antibiotics in some situations. Honey was reported to be highly effective in promoting healing and as an analgesic agent when administered intraoperatively to and consumed postoperatively by children who underwent tonsillectomy. Chlorhexidine-containing intraoral medications are used extensively in the treatment of various oral diseases, particularly oral bacterial and fungal infections. However, chlorhexidine use has limitations because of unacceptable effects such as an unpleasant taste and tooth staining. One variety of honey exhibited significant bactericidal activity against multiple oral pathogens that colonize oral biofilms. The microorganisms responsible for oral diseases that have been reported to be inhibited by honey include *S. mutans*, *Actinomyces viscosus*, *S. sobrinus*, *Fusobacterium nucleatum*, and *P. gingivalis*. In particular, manuka honey from New Zealand exerted a strong bactericidal effect on *S. mutans*. In addition, manuka honey restricted the growth of *S. mutans* on saliva-coated hydroxyapatite disks and glass surfaces. These findings indicate the anticariogenic and antimicrobial potential of honey. This potential can be utilized as an alternative to conventional treatments such as chlorhexidine.<sup>24</sup> Based on its clinical effectiveness, manuka honey dressing is used as the first-line therapy for infected maxillofacial wounds at the Maxillofacial Unit of the Royal Surrey County Hospital, Guildford, Surrey.<sup>25</sup> Honey alone or as an adjunct therapy was reported to effectively minimize the oral complications and weight loss associated with chemotherapy or radiotherapy if used regularly either during or after these therapies. The administration of honey was reported to

minimize the severity of oral mucositis in patients with oral cancer who underwent simultaneous radiotherapy and chemotherapy. Furthermore, honey has also been reported to expedite healing and reduce the occurrence of oral fungal infections. Moreover, honey has been reported to reduce the incidence of caries by reducing colonization by *S. mutans* in patients with radiation-induced xerostomia.<sup>21,26,27</sup> The inhibition of dental calculus formation is central to the prevention of oral diseases such as gingivitis and dental caries. Dentifrices containing zinc chloride and pyrophosphate are currently available as anticalculus agents. These agents check calculus formation by actively inhibiting the calcium phosphate precipitation from saliva. However, these dentifrices are also associated with adverse effects that are specific for synthetic chemicals. An in vitro investigation to screen for the formation of calcium phosphate precipitates was performed using 20 varieties of honey. The results revealed that 6 varieties of honey reduced the rate of transformation of amorphous calcium phosphate to hydroxyapatite by 12% to 35%. These results indicate that honey may be used as anticalculus agent in mouthwashes and toothpastes.<sup>28</sup>

Ten percent formalin is used as a fixative agent in diagnostic histopathology. The fixation of biopsy specimens facilitates the processing of the specimens for microscopic examination and for archival preservation. However, the disadvantage of formalin use is that it is a potential carcinogen. Hence, identifying a safer alternative is necessary. A specimen preserved in honey for almost a month did not exhibit any indications of autolysis and putrefaction; thus, honey inhibits autolysis. Honey also hardens the biopsy tissue specimen. Chemical fixatives also act by hardening the tissues. In a study that compared the fixative properties between honey and formalin in oral tissues, the tissue morphology and staining efficiency of the honey-fixed oral tissue specimens were similar to those of the formalin-fixed specimens. This finding suggests that honey is reliable and is a safer fixative than formalin.<sup>29</sup>

Dry socket or alveolar osteitis is a common complication arising after dental extraction. It occurs because of the dislodgement of the blood clot in the extraction socket. Consequently, the bone and nerve are exposed to anything entering the mouth such as, food, fluids, and air. Patients with dry socket experience severe pain that can last for a week. In a study on patients with dry socket, the application of a honey dressing to the extraction wound site considerably reduced pain and inflammation. Honey dressing also prevented infection

of the extraction wound site, thus resulting in expedited wound healing. Excessive application of eugenol, the standard treatment for dry socket, can lead to bone necrosis; however, the honey dressing did not cause any adverse effect. These findings indicate that honey is a safe and natural dressing for management of dry socket.<sup>30</sup> Studies have shown that eating raw honey is safe and does not cause oral health hazards such as dental decay and gum problems. A significant reduction in plaque deposition was reported in volunteers who chewed “honey leather” made from manuka honey. This finding suggests a potential role of honey in improving oral health.<sup>31</sup>

**Propolis.** *Candida albicans* can become pathogenic through various virulence factors. Among these virulence factors, the ability to convert from the yeast to the hyphal form is the most crucial factor in the pathogenicity of the organism. *Candida albicans* isolated from oral lesions was sensitive to propolis ethanolic extract (PEE) because PEE targeted the conversion of the yeast to the hyphal form.<sup>32</sup> Moreover, in denture wearers who exhibited denture stomatitis or oral candidiasis, the antifungal effect of propolis was comparable with that of a local antifungal agent, namely miconazole. Therefore, propolis may be a natural preventive and therapeutic agent against oral candidiasis. Studies have demonstrated that administration of propolis capsules to patients with recurrent aphthous ulcers significantly reduced the soreness and frequency of ulcer recurrence in these patients.<sup>21,33</sup> A double-blind clinical trial reported that the use of a propolis-containing mouthwash (10% tincture diluted 1:5 with water) provided significant relief to patients with gingivitis.<sup>34</sup> In addition, propolis was found to effectively reduce the growth of microbes involved in periodontal pocketing and with bleeding on probing, such as *Tannerella forsythensis*, *P. gingivalis*, and *Treponema denticola*. The phenols and flavonoids present in propolis are believed to be responsible for the activity against periodontal pathogens. Propolis was also reported to reduce halitosis or bad breath. This effect is due to the action of propolis against odor-causing bacteria, particularly *P. endodontalis*, *Prevotella intermedia*, and *Eubacterium spp.* However, propolis is less effective than lavender, zinc, and echinacea in reducing halitosis. An extract made from various components from propolis exhibited an antiviral effect against herpes simplex virus involved in ulcerations affecting the oral region.<sup>33</sup> The antimicrobial action of propolis is attributable to the flavonoids and esters of phenolic acids present in it.<sup>35</sup> Maintenance of oral

hygiene is critical for normal healing of postoperative oral wounds. Poor oral hygiene in patients with mandibular fractures may lead to a complication of osteitis arising from infection in the fracture crevices. The use of a gel containing an ethanolic extract (3%) of Brazilian green propolis resulted in superior management of oral hygiene in patients with mandibular fractures compared with the controls. Propolis gel eliminated pathogenic and opportunistic microbes without adversely affecting the physiological microflora.<sup>36</sup> Limiting the formation of dental plaque is central to the prevention of dental caries. Propolis was reported to retard calcium phosphate precipitation; hence, it potentially checks the buildup of dental plaque.<sup>33</sup> Notably, propolis was reported to exert a cariostatic effect in rats. This effect was believed to be due to the high fatty-acid content of propolis, which reduces acid production by and acid tolerance of *S. mutans*.<sup>37</sup> Although propolis-based mouth rinses were not as efficacious as chlorhexidine gluconate mouth rinses in the prevention of caries in humans, their effects on gingival fibroblasts were less cytotoxic than were those of chlorhexidine. This safety feature justifies the use of propolis-containing mouthwashes. In restorative dentistry procedures, direct pulp capping with propolis stimulates the dental pulp to form restorative dentin. Moreover, propolis and calcium hydroxide were reported to exert similar beneficial effects on the healing of inflamed pulp and stimulation of reparative dentin. Propolis also has the potential to counteract tooth sensitivity because it seals the dentinal tubules.<sup>33</sup> A successful endodontic treatment is based on the complete removal of bacteria from root canals. The main obstacle is *Enterococcus faecalis* (*E. faecalis*), which may withstand the effects of some root canal medicaments. As an intracanal medicament, a 30% solution of propolis was more effective in decontamination of *E. faecalis* from the root canals than nonsetting calcium hydroxide paste.<sup>38</sup> Orthodontic appliances may be associated with an increased accumulation of dental plaque and impairment of gingival health. The use of a propolis-containing toothpaste improved oral hygiene and reduced gingival inflammation in individuals with orthodontic appliances during a 35-day study period.<sup>39</sup> An inflammatory reaction induced by dental plaque in tissues surrounding dental implants may compromise the integrity of the tissues. The use of a propolis-containing toothpaste considerably improved oral health and reduced plaque-induced gingivitis in individuals with dental implants. Based on these results, propolis may be considered an alternative treatment for

the management of periodontal problems in individuals with dental implants. However, for superior treatment compliance, the products containing propolis should have appropriate organoleptic properties, such as color, odor, and taste.<sup>40</sup>

All these findings suggest that propolis preparations can be useful subsidiary treatments in various oral diseases and conditions. The benefits of propolis in oral health can be derived by incorporating it in oral care preparations such as toothpastes, mouthwashes, and prophylactic gels.

**Royal Jelly.** Dental injuries due to accidents or violence may result in complete dislodgement of teeth from the alveolar sockets. This phenomenon is known as avulsion. The optimal treatment option for an avulsed tooth is replantation in its socket as soon as possible. If immediate placement is not possible, the avulsed tooth should be placed in a proper storage medium to maintain the viability of the cells of the periodontal ligament (PDL) because the PDL cells exhibit regeneration potential that is considered essential for successful replantation. In an in vitro tooth avulsion model, RJ solution was more effective for the storage and transportation of avulsed teeth than milk or Hank's balanced salt solution.<sup>33,41</sup>

**Berries.** Berries are a rich source of various nutrients and phytochemicals that protect from various diseases. Berries are consumed in a variety of forms, such as fresh, dried, frozen, and canned. Various types of berries include strawberry (*Fragaria ananassa*), red raspberry (*Rubus idaeus*), black raspberry (*Rubus occidentalis*), blackberry (*Rubus sp.*), blueberry (*Vaccinium corymbosum*), cranberry (*Vaccinium macrocarpon*), and grapes (*Vitis vinifera*). The nutritional and therapeutic value of berries is because of their high content of antioxidants, polyphenols, minerals, and vitamins.<sup>42</sup> The antioxidant activity of polyphenols inhibits and modulates various receptors, transcription molecules, and enzymes involved in infection, malignancy, inflammation, and neurodegeneration.<sup>43,44</sup> Dental plaque development is caused by interspecies adhesion or coaggregation. In dental plaque, *S. mutans* aggregates with *Fusobacterium nucleatum* or *Actinomyces naeslundii*. Results from an in vitro study indicated that the polyphenols in the high-molecular-size fractions of crowberry, blackcurrant, bilberry, and lingonberry juices exerted an antiaggregation effect on plaque colonizers. Anthocyanins, proanthocyanidins, and flavonol glycosides are the polyphenols that play a role in antiaggregation.<sup>45</sup> Among the tested polyphenol-containing fruit extracts, red and green grape extracts

exhibited the highest inhibition activity against *S. mutans*. Moreover, grape seed extracts were more effective as inhibitors than grape skin extracts. The red grape seed extracts exhibited higher activity against *S. mutans* than the green grape seed extracts.<sup>46</sup>

Cranberry juice is well known for its use in the prevention of urinary tract infections. This effect is due to the inhibition of adhesion of *Escherichia coli*. Based on this property, cranberry juice can act as an anticariogenic agent by potential inhibition of *S. mutans*.<sup>44</sup> Cranberry was the only fruit among the polyphenol-containing fruits that efficiently and steadily inhibited the formation of oral biofilms. Treatment with cranberry juice interfered with the adhesion of *S. mutans* and *S. sobrinus* cells because it reduced the cell-surface hydrophobicity.<sup>47</sup>

In oral biofilms, increased metabolic activity creates an acidic environment. However, *S. mutans* can maintain an alkaline intracellular pH through the removal of protons by using the F-ATPase proton pump. Notably, proanthocyanidins and flavonols from cranberry have been demonstrated to inhibit the activity of microbial F-ATPase, thus making bacterial survival extremely challenging.<sup>48,49</sup>

Raspberry leaf extract (RLE) has been used by Western herbalists as an empirical therapy for various oral mucosal conditions including swollen gums and sore mouth. The main constituents of RLE that are potentially responsible for its health benefits are tannins and 2 flavonoids, namely quercetin and kaempferol. Oral lichen planus (OLP) is a chronic mucocutaneous inflammatory disease. A majority of patients with OLP complain of oral discomfort in the form of a burning sensation and soreness. In an Australian investigation, RLE was found to be an efficacious and safe in OLP treatment. The use of RLE significantly reduced the clinical features of OLP such as burning sensation, reticulation, erosion, and ulceration. In Australia, RLE has been approved as a safe herbal product.<sup>50</sup>

Black raspberries are a rich source of antioxidants and chemopreventive phytochemicals. Among these are anthocyanins, which are present in appreciable quantities in black raspberries. Treatment of cell lines isolated from human OSCCs with an ethanolic extract of freeze-dried black raspberry significantly suppressed numerous biochemical reactions involved in cancerous transformation. These findings indicate that black raspberry can play a promising chemopreventive role by inhibiting OSCC transformation in oral epithelial dysplasias. In individuals with oral dysplasia, dietary administration of freeze-dried black raspberries may be a crucial factor in life-long chemoprevention.<sup>51,52</sup>

Raisins, the dried form of grapes, possess phytochemicals (oleanolic acid, oleanolic aldehyde, linoleic acid, linolenic acid, botulin, and betulinic acid) that are beneficial to oral health because of their antimicrobial action against oral pathogens responsible for causing caries or periodontal diseases. Proanthocyanidins contained in grape seed extract have a positive effect on the demineralization and/or remineralization of artificial root caries lesions. These beneficial effects of various berries indicate their potential as promising natural agents for the management of various oral microbial diseases.<sup>53</sup>

**Olive oil.** Olive oil is an integral component of Mediterranean cuisine. Compelling evidence has highlighted the beneficial effects of olive oil on oral health. Massaging the gums with olive oil for 10 minutes daily for 3 weeks significantly reduced the *S. mutans* and *Lactobacillus spp.* counts as well as plaque scores. This reduction was comparable to that caused by chlorhexidine gel. However, in contrast to chlorhexidine, olive oil is reasonably priced and readily available. Because of affordability and accessibility, this finding suggests the valuable potential of olive oil in enhancing oral hygiene in patients with low socioeconomic status.<sup>54</sup>

Oral dryness may occur as a side effect of various medications. A study for assessing the effectiveness of topical oral preparations, namely a toothpaste, mouthwash, and gel, containing olive oil as one of the ingredients was performed in patients with drug-induced oral dryness. The results revealed a significant improvement in salivary flow rates following the use of these topical products. Moreover, their use led to a considerable improvement in the quality of life in patients with drug-induced xerostomia. Most importantly, no adverse effects were observed on using these topical agents containing olive oil.<sup>55</sup>

Burning mouth syndrome (BMS) is a chronic disorder of unknown etiology characterized by burning sensation in the oral mucosa. After a 12-week intraoral application of lycopene-enriched olive oil, patients with BMS reported significant alleviation of pain and burning sensation. Moreover, the oral quality of life of the patients was reported to improve. Most importantly, no side effects of using lycopene-enriched olive oil were reported. By contrast, numerous side effects are associated with conventional medications used for managing BMS, such as anxiolytic drugs, antidepressants, alpha-lipoic acid, sialogogues, topical anesthetics in rinses, and anticonvulsants. These results suggest that lycopene-enriched olive oil can be a safe, natural, and novel treatment alternative for managing BMS.<sup>56</sup>

In conclusion, considerable evidence suggests the potential of natural substances in the development of pharmaceutical preparations with a prophylactic or therapeutic role in oral diseases. Additional randomized and extensive clinical trials of the safety and efficacy of these agents are warranted. Positive findings from such studies will consolidate the evidence of the beneficial effects of natural substances on oral health available thus far.

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