EXPERT VIEW/REVIEW PAPER

Chewing Gum for Oral and Dental Health: A Review

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Abstract

Background: The widespread use of chewing gum has spurred interest in the use of chewing gum as a vehicle for a variety of drug delivery systems. Medicated chewing gum is an ideal dosage form for frequent dosing at low concentrations and has advantages due to ease of use and better human compliance. In dentistry, fluoride (F), chlorhexidine (CHX), calcium phosphate, and other mineral and metal salts are added to chewing gums.

Aims and objectives: This review aims to highlight and update the use of chewing gum to promote oral and dental health based on published data over the past 40 years.

Materials and methods: A thorough literature search was performed using appropriate keywords, including previous literature reviews.

Results: Literature analysis shows the following five benefits: (1) Chewing gum strongly increases saliva flow and volume through mechanical action and the flavors it contains. (2) Saliva and its various constituents play an essential role in the protection of the teeth and oral health, by clearance of sugars and food debris; neutralizing plaque pH after a sugar challenge; promoting remineralization of early caries lesions, and allowing frequent topical application with relatively low therapeutic dose. (3) Sugary chewing gum proved to be cariogenic. (4) Sugar-free chewing gum with F and CHX is an important adjunct in inhibiting dental caries, decreasing plaque formation, and reducing gingivitis scores. (5) Chewing gum is a safe product with no adverse effects.

Conclusion: The oral and dental benefits of sugar-free chewing gum have been confirmed by the International Dental Associations, Authorities, and Federations.

Clinical implication: Adding sugar-free chewing gum to routine oral care of brushing with fluoridated dentifrice and interdental cleaners can reduce the risk of caries and gingivitis.

Keywords: Caries, Chewing gum, Chlorhexidine, Fluoride, Periodontal disease, Sugar-free, Sugar substitute, Xerostomia.

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Introduction

Chewing gum is one of the most common candies all over the world, especially among teenagers. It is estimated that the global chewing gum market is about 560,000 tons per year, worth about 5 billion US dollars, and the global chewing gum sales are about 374 billion sticks per year.[1] Drug delivery vehicles with short treatment cycles and low side effects have always been an attractive target in the fields of medicine and pharmaceuticals. Among them, chewing gum is proven to be promising in carrying drugs for dental and oral health, which has the advantage of high individual compliance compared to other oral pharmaceutical products. Water-soluble substances in chewing gum are released rapidly and completely, and methods of delaying their release to provide a prolonged release profile may be used. Gum bases are often hydrophobic, which can alter the release rate of the loaded drug.[2] The basic ingredients of chewing gums are gum base (25–35%; polymers, plasticizers, and resins); sweeteners (40–50%; sugar alcohols (sorbitol, xylitol, or mannitol); softeners (2–15%; glycerin or vegetable oil), flavors (1.5–3%; mint, fruit, spearmint, menthol), and color.[3] Softeners are used to blend other ingredients and prevent the gum from becoming hard or stiff. Bubble gum contains more of the gum base and softener.

Nicotine-containing gum (Nicorette®) was the first medicated chewing gum, marketed in Switzerland (1976) for smoking cessation. Nicotine is transported into the bloodstream through absorption by the oral mucosa. To date, various therapeutic agents have been introduced in chewing gum for dental oral health including:

- Antiplaque/antibacterial (chlorhexidine (CHX), eucalyptus, mastic, xylitol, sodium bicarbonate, zinc acetate).
- Anticaries (fluoride; calcium phosphate; CHX).
- Antigingivitis (CHX, hydrogen peroxide; sodium bicarbonate; vitamin C; eucalyptus; green tea).
- Anti-oral candidiasis (Nystatin; Clotrimazole; Fluconazole).
- Teeth whitening (hydrogen peroxide; carbamide; sodium bicarbonate; citric acid; malic acid; silica).
- Anti-hyposalivation (mint flavor; sorbitol/xylitol; methylcellulose).

Chewing gums labeled as "Safe for teeth" or "Tooth-friendly" in Europe or "Happydent" in Brazil are sweetened with sugar substitutes, mainly sorbitol, xylitol, or mannitol. According to the American Dental Association (ADA), adding sugar-free (sugarless, or no sugar) chewing gum to twice-daily brushing with fluoridated toothpaste and interdental cleaning reduces caries risk.[4] As adjunct, to toothbrushing, sugar-free chewing gum is helpful for the control of dental plaque (dental biofilm) formation and gingivitis. This overview presents published clinical research on the use of chewing gum in dentistry over the past 40 years.

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Chewing Gum

The mechanical action of the chewing gum stimulates the salivary glands to produce a high saliva flow rate and increases the pooled saliva volume. The flavors in the gum further stimulate saliva by triggering taste receptors in the mouth. The most important functions of saliva with respect to caries are its role in the removal of bacteria and food debris from the mouth, inhibiting plaque formation, neutralizing plaque acidity, promoting remineralization of early enamel lesions, control enamel demineralization, antibacterial action, maintaining environment saturated in calcium, phosphate, and providing a buffering system (bicarbonate, phosphate, and protein), with bicarbonate (HCO_3-) the most important buffer.[5–7] Reviews of clinical studies have indicated that chewing sugar-free gum after meals and sugared snacks results in a significant reduction in the formation of dental caries.[1,8,9] Chewing gum is also recommended for people with poor oral hygiene, persons with physical and mental disabilities, patients with rapid progression caries, and low salivation, such as those receiving radiation therapy.

Sugar-containing Chewing Gum

Contrasted to beneficial sugar-free gum, clinical trials have shown that sugar-containing gum can increase the incidence of dental caries by increasing plaque growth, adhesion, and acidity. Sucrose is readily metabolized by oral cariogenic bacteria, causing a greater drop in plaque pH than any other carbohydrate. Chewing sugary gum, may cause the plaque pH to drop below the critical pH 5.5, where enamel minerals begin to dissolve. Individuals prone to caries are more susceptible to plaque pH drops than those who are more resistant to plaque fluctuations following sugar intake. In addition to the cariogenicity of sucrose in some gums, their physical consistency, oral retention time, and frequency of use are contributing factors. Research shows that chewing gum for 5 days reduces plaque buildup and saliva debris by 50%. It was noted that the removal of plaque during brushing occurred mainly away from the gum margins and interdental areas where dental caries and gingival inflammation mainly happened.[10] Several clinical studies have evaluated the effect of chewing sugar-containing gum on plaque formation. Ainamo et al. found that chewing gum sweetened with sucrose significantly promote plaque growth and significantly increased the number of bacterial deposits, while chewing sorbitol gum during a time period of 3 hours did not reduce the plaque scores.[11] A clinical trial was conducted on schoolchildren aged 9–11 years. One group of children received no chewing gum as a control group, while other groups of children received gum sticks containing either sucrose, sorbitol, or xylitol five times a day. At the end of the 40-month trial, children who chewed the sucrose-containing gum had an increased caries incidence than children who received no chewing gum. In contrast, children who chewed sorbitol-containing gum had a 20.8% decrease in caries incidence compared to the control group. A greater reduction in caries was observed in the xylitol group; ranging from 43 to 71% when compared with the sucrose and control groups.[12]

Sugar-free Chewing Gum

According to the US Code of Federal Regulations, 2022 (21CFR101.60) food and chewing gum can be labeled as "sugar-free" if it contains less than 0.5 g of sugars per serving. In place of sugar, gums are sweetened with sugar alcohols (polyol) such as sorbitol, xylitol, or mannitol. To a lesser extent, high-intensity sweeteners such as acesulfame-K, aspartame, neotame, saccharin, or sucralose are also used. Unlike sugar, these sweeteners are not metabolized by bacterial plaque, with the exception of sorbitol and mannitol which metabolized slowly. Sorbitol is widely distributed in the plant kingdoms such as berries, apples, plums, pears, etc., and was introduced into the diet of diabetics as early as 1929. Sorbitol is commercially produced from sucrose or starch and is about one-half as sweet as sucrose with one-third fewer calories. It is used as a sugar substitute in confections, chewing gums, chocolates, jams, jellies, and others; labeled as a "dentally safe" sweetener. Sorbitol is also used in the formulation of oral care products such as toothpaste and mouthwash. Xylitol is found in small amounts in fruits and vegetables, such as bananas, strawberries, cauliflower, and mushroom, and is commercially produced from coconut shells, birch trees, and xylan-containing wood. Its sweetness equal to that of sucrose (table sugar). Xylitol is 10 times more expensive than sucrose and has 40% fewer calories. To reduce production costs, xylitol is produced from corn cobs. As sorbitol, xylitol is used in many foods and confectionery. Oral microorganisms, especially *S. mutans*, do not possess enzymes to use xylitol as a source for acid production and synthesis of extracellular polysaccharides to form plaque deposits. Sugar-free chewing gum first entered the market in the early 1950s. Today, synthetic materials have replaced natural gum ingredients to provide chewing gum with better quality, texture, and taste.

Literature Reviews

Numerous clinical trials have evaluated the effectiveness of chewing gum for oral and dental health. A review of 19 articles showed that the use of xylitol, a xylitol-sorbitol blend, sorbitol, and sorbitol-mannitol blend was associated with mean caries prevention rates of 58, 52, 20, and 10.7%, respectively.[13] A review of nine articles showed that two of them did not find a caries-preventive effect of sugar-free gum, while the remaining articles showed that chewing sorbitol, xylitol, or sorbitol-xylitol sweetened gum was caries-preventive.[14] Burt reported that chewing sorbitol gum three times a day was less cariogenic than sugar gum, while xylitol gum was not cariogenic in all protocols tested.[15] Some studies in this review claim that xylitol-sweetened chewing gum have antibacterial effects, including . The use of chewing gums containing either xylitol, sorbitol, or a mixture of both for two years resulted in a significant decrease of caries incidence in primary dentition, with a reduction in the xylitol and sorbitol gum groups was 35 and 44% compared to the no-gum group. The xylitol-sorbitol mixtures were less effective than xylitol, but they significantly reduced caries rates compared with the no-gum group.[16] In a caries prevention program involving the use of xylitol chewing gum in children aged 13–14 years, Isogangas et al.[17] found that children who used xylitol gum daily have significantly lower caries scores compared to the control group (no chewing gum). After 5 years of discontinuation of the gum program, the difference in caries incidence had continued to increase in favor of the xylitol group.

In a systematic review of 12 studies on adults and children, Newton et al. (2020) revealed that the group who chew xylitol gum alone had a reduced caries increment by 33%, compared to a 28% caries reduction in those who do not chew sugar-free gum or use alternatives such as lozenges, candies, rinses, tablets, and other non-chewing items.[9] Another literature review showed that chewing gum sweetened with xylitol reduced dental caries more than gum sweetened with sorbitol and that sucking candies or

tablets containing xylitol had the same effect as chewing xylitol gum.[18] A two-year study on Danish school children aged 8–12 years who chewed a piece of sorbitol-containing gum after each meal showed that caries increments increased by 5.6 surfaces compared to 6.2 in the control group who did not eat gum.[19] An *in-situ* study of remineralization of artificial caries-like lesions in which subjects chewed sorbitol gum 20 minutes after each meal or snack showed significant (doubled) remineralization of the lesions, compared to pre-chewing values.[20] A systematic review (2021) of 13 studies in adults and children showed that xylitol chewing gum significantly reduced the *S. mutans* of effect compared with no-gum chew, or received probiotics and F varnish.[21] A study was conducted on participants who did not brush the teeth in the lower jaw designated to develop experimental gingivitis while maintaining normal oral hygiene procedures in the upper jaw. After chewing xylitol or maltitol gum for 10 minutes, 5 times a day for 3 weeks, marginal probing bleeding and plaque scores were significantly ($p < 0.001$) lower compared to chewing gum base in the absence of toothbrushing.[22] One review showed that xylitol chewing gum significantly reduced gingivitis scores compared with no gum or gum-basis chewing. Sorbitol chewing gum showed a slight decrease in gingival scores, while maltitol was less effective.[23] From accumulated studies it can be concluded that habitual use of xylitol gum as an aid to brushing is effective in removing dental biofilm and reducing gingival inflammation.

Fluoride Chewing Gum

The frequent use of products with low fluoride (F) concentration, with active F delivery to the enamel-plaque-saliva biosystem can promote the remineralization of early carious lesions. Fluoride-containing chewing gum fits into this anticaries concept. Studies have shown that there is no simple cause-and-effect relationship between the F content of dental products and their anticaries effects.[24,25] The release of F from dental materials occurs through three different mechanisms, namely: surface dissolution (washout); diffusion through microchannels and pores, and bulk diffusion. Several intrinsic and extrinsic factors governed F release in the oral cavity including the material structure, physical and chemical properties, composition, permeability, type and content of F compounds, nature of saliva (pH, flow, viscosity, F-complexing ions), and other oral environmental conditions. Besides factors involved in F release *in-vivo*, the F-releasing rate *in-vitro* is influenced by powder/liquid ratio, mixing time, temperature, specimen geometry, surface area, F complex with secondary ingredients, type, and volume of the storage medium, frequency of medium change, and stirring.[26] Fluoridated gum is unique in its effectiveness by mechanically degrading the gum material and increasing saliva flow during chewing, resulting in rapid dissolution of the F-compound and complete release of F^-. However, there are ways to delay drug release from chewing gum to provide an extended-release profile.

Bruun and Givskov[27] found that chewing gum containing 0.25 mg F released 11.7, 15.3, and 3.9 ppm, after 2-, 5-, and 10-minutes of start chewing, and still higher than the resting value (0.05 ppm F) after 60 minutes. The residual F content in the gum after 10 minutes of chewing was 6% of the initial 0.25 mg. In another study, these authors assessed salivary F concentrations released from F chewable tablets (0.21 mg F) or F-containing chewing gum (0.25 mg F) and high doses (0.42–0.50 mg F). Peak F was reached within 5 minutes of initiation of chewing at levels of 15–25 ppm for the low-dose group and 25–40 ppm for the high-dose group. They indicated that chewing gum provided significantly more F in saliva than the chewable tablets.[28] Sjögren et al.[29] assessed salivary F clearance after gum chewing (Fluomin and Fluorette), and sucking tablets (Dentan and Fluent), all containing 0.25 mg F as NaF. Gum chewing continued for 5 min and the tablets until completely dissolved in the mouth. The results indicated that chewing gum and tablets had about the same clearance pattern in saliva and the same salivary-stimulating effect. In other studies, they reported that the area under the curve (AUC) of salivary F concentrations in chewing gum containing 0.25 mg F, after 1-minute rinsing with a 10% sucrose solution, was 2–3 times higher than that of the non-chewing side. Prolonged chewing significantly increases plaque pH.[30] A comparative study between chewing gum containing 0.50 mg F and two tablets containing 0.25 mg F (as NaF) showed no significant differences in saliva F concentrations between the gum and the tablet, suggesting that F-gum could be a valid alternative to the use of NaF tablets in caries prevention.[31]

Few publications provide the clinical effects of F chewing on enamel remineralization and caries prevention. *In-situ* enamel sections with subsurface lesions, was mounted in removable lower appliances, and subjects chewed five sticks/day of F gum (0.1 mg F/stick) for 3 days. The results showed a significantly higher microhardness value of the test group than those of the control group chewing non-F gum.[32] Another *in-situ* test, with sections of early root lesions were mounted in removable lower appliances. The test group chewed five sticks/day (0.1 mg F/stick) for 21 days, while the control group used F-free dentifrice. Significantly higher rate of remineralization and F uptake was found in the test group compared to the control group.[33] Hattab et al.[34] were the first to study the effects of F-containing chewing gum on the remineralization of incipient caries lesions, plaque F uptake, and safety. The following are the local and systemic effects of F chewing gum.

Salivary F Release

Healthy adults refrained from brushing with F-toothpaste for 3 days and not consume F-rich foods and drinks. Subjects chewed a stick of sugar-free Fluogum® (containing 0.113 mg F as NaF) for 15 minutes. Saliva samples were collected for 1minute into plastic containers at intervals of 2, 5, 10, 15, 30, 45, 60, 120, and 180 minutes during and after the chewing procedure. No attempt was made to interfere with the subject chewing or swallowing habits. The volume of expectorated saliva was measured using automatic pipettes. On the latter occasion, the above procedure was repeated using two sticks of Fluogum® (containing 0.23 mg F) chewed simultaneously. Fluoride analysis was performed using an F-ion electrode coupled to a microprocessor ion analyzer (Orion, Cambridge, Massachusetts). Prior analysis, samples were buffered with 10% by volume of acetate buffer containing 2% CDTA. After chewing a stick of Fluogum®, salivary F concentrations rose from 0.03 ppm (pretreatment or resting value) to a peak of 1.2 ppm after 5 minutes of chewing; that is, 40 times higher than the resting value. The corresponding peak F concentration after chewing two sticks was 2.73 ppm, i.e., 91-times higher than the resting value (Fig. 1). The area under the curve (AUC) of salivary F concentration versus time was 0.78 h × μg/mL and 1.89 h × μg/mL after chewing one and two sticks, respectively. The mean saliva flow rates for one and two sticks after chewing for 5 minutes were 2.1 ± 0.75 and 2.8 ± 0.40 mL/min, respectively (± SD), respectively. There was a high positive correlation (r = 0.78) between salivary flow rates and F clearance.[34]

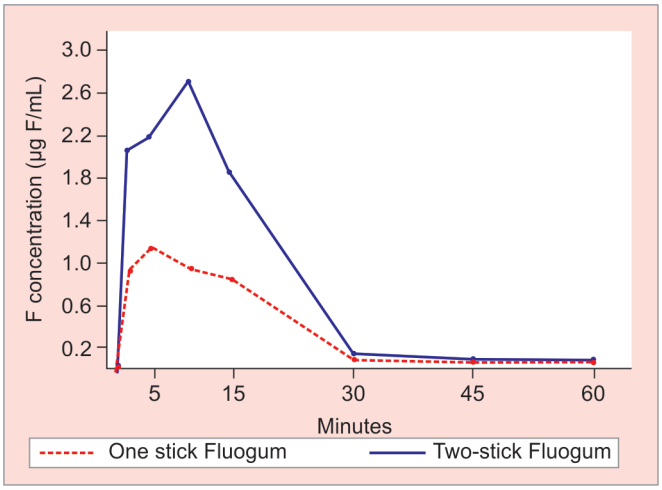


Fig. 1: Mean F concentration (µg/mL) in whole saliva at different time intervals during and after 15-minutes of chewing one or two gums containing 0.23 mg F (as NaF) each. The peak salivary F occurred 5 min after chewing one stick of Fluogum®, and 10 min after chewing two sticks

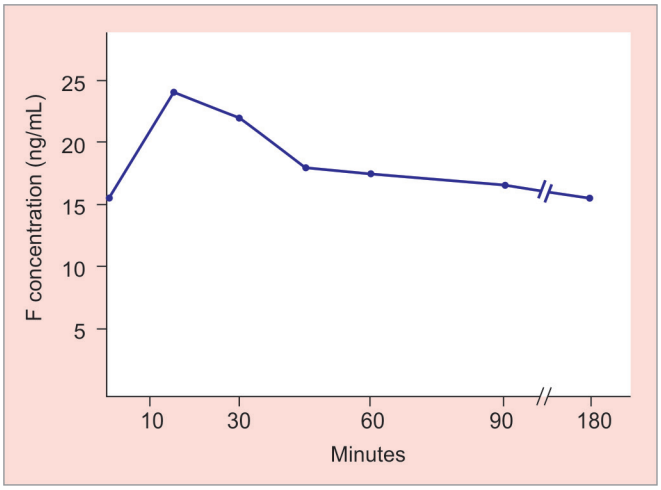


Fig. 2: Plasma F concentration (ng/mL) while chewing two gum sticks each containing 0.23 mg F (as NaF)

Plaque F Uptake

Before chewing the gum, baseline plaque samples were collected from all accessible sites using a plastic spatula. The subjects then chewed two sticks of Fluogum for 15 minutes. The plaque was sampled after 1 and 3 hours. The average amount of plaque sampled was 7.8 mg. Excess saliva was blotted out of the plaque with F-free filter paper. The sampled plaque from each subject was transferred to preweighed microcentrifuge tubes, and the wet weight was recorded to the nearest 0.01 mg. The plaque was suspended in 0.250 mL of 0.5 $HClO_4$ and dispensed using a vortex mixer. Extraction of F was carried out at room temperature for 12 hours. Chewing gum increased F levels in plaque from 2.94 ± 1.02 to an average of 4.87 ± 2.26 µg/g at 1hour after chewing, and still about the same concentration after 3 hours. There was a positive correlation between F levels in saliva and plaque.

Plasma F Levels

The plasma F experiment was performed on an adult living in an area with 0.7 ppm F in drinking water. After overnight fasting, the subject was given two sticks of Fluogum to chew for 15 minutes and to swallow the pooled saliva. Fingertip blood samples were collected before chewing gum and after 15, 30, 45, 60, 90, 120, and 180 minutes after chewing gum. Blood samples were placed in microcentrifuge tubes containing 5 µL of F-free heparin to prevent blood clotting and centrifuged at 12,000 g for two minutes. Plasma F levels rose slightly from 16 ng/mL (Baseline value) to a peak of 24 ng/mL. After 20 minutes of chewing it returns to pre-chewing value at 2 hours (Fig. 2). AUC was 6.3 h × ng/mL.

Remineralization

The remineralization process can control the progression of caries by inhibiting and reversing early enamel demineralization. In this process, functional F guides the deposition of minerals on the damaged enamel. Remineralized enamel caries can lead to distinct optical changes in the lesion. Mineral volume changes arising from remineralization can be measured based on the optical reflectivity of the lesion (birefringence). Calculations of

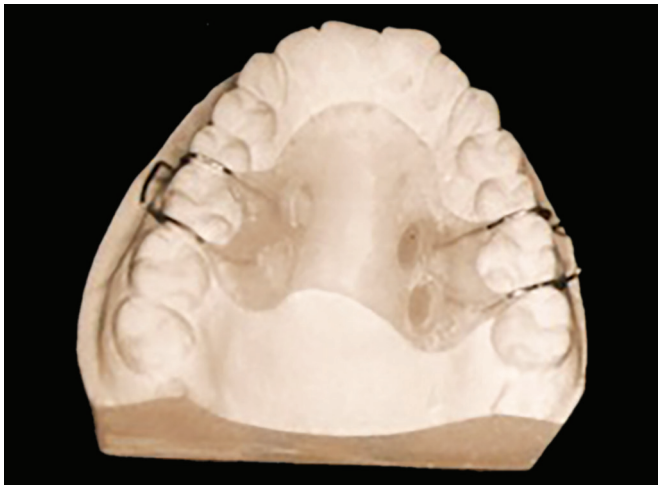
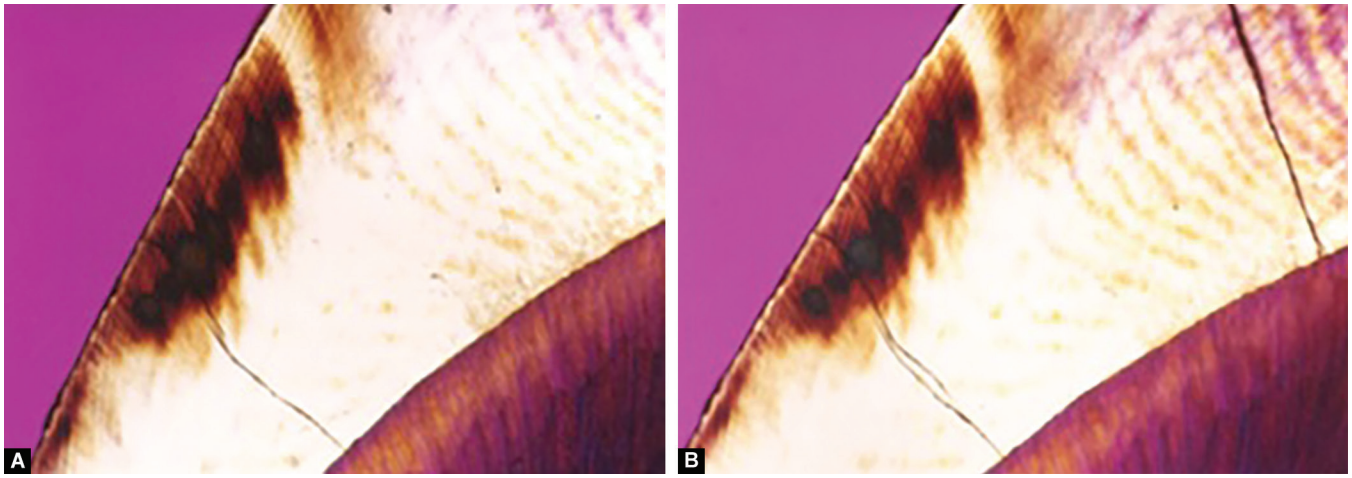


Fig. 3: Carious enamel sections embedded in the maxillary acrylic appliance with the outer surface of sections is exposed to the oral environment

birefringence are derived from the ray's difference between the lesion and the sound structure. The more the volume of the enamel pores (as in the demineralization process) the higher the positive birefringence value and vice versa for the negative birefringence. *In-situ* remineralization of enamel sections with white spot carious lesions was assessed in subjects after 3 days of chewing 15 sticks of Fluogum®.[34] Subjects lived in a community with fluoridated water (0.7 ppm) and wore maxillary acrylic appliances in which carious enamel sections were embedded (Fig. 3). Birefringence values of pre- and post-chewing were assessed using polarized light microscopy (PLM). After the test period, there was a significant reduction in both lesion depth and in the lesion body size ($p < 0.001$); a reduction of 10 and 28%, respectively (Fig. 4). In a separate experiment, the same procedure was performed, except that the subjects chewed F-free gum. Findings revealed no marked reduction of the lesion depth, but significantly reduced the lesion body by an average of 5%. This could be related to the mechanical



Figs 4A and B: Remineralization effect of chewing F gum: (A) A typical carious lesion in enamel viewed in polarized light after imbibition in water. The lesion shows a negatively birefringent surface zone superficial to the positively birefringent body of the lesion; (B) The same lesion of (A) after exposure to F-gum for 3 days, and examined under identical conditions to that in (A). Note increased remineralization of the outer surface and body of the lesion.

chewing action on stimulating salivary flow that provides high Ca^{2+} and PO_4^{3-} levels essential for remineralization.[34,35]

Chlorhexidine Chewing Gum

Chlorhexidine (CHX, commonly known as chlorhexidine gluconate), is a strong disinfectant and antiseptic agent widely used as a broad-spectrum antimicrobial agent effective against gram-negative and gram-positive aerobes and anaerobes bacteria and fungi. It has a cationic molecular component that attaches to a negatively charged cell membrane, causing cell lysis. Due to its ability to adhere to hard and soft tissues with long-lasting effects, CHX is used by hospitals and clinics for cleaning the skin or surgical equipment prior to surgery and for skin treatments in the form of creams, ointments, and lotions. In the field of dentistry, CHX alone or in combination with F is used in mouthwash, gel, lozenge, spray, varnish, toothpaste, dental floss, toothpick, etc., as antiplaque, anticaries, and antigingivitis. Co-administration of CHX and F showed higher diffusion in human enamel than in administration alone.[36] The synergistic effect of CHX with F in caries prevention has been demonstrated.[37] Corsodyl® and Hexidine® contain 0.2% chlorhexidine. Peridex®, Oradex® contains 0.12% CHX. The anti-plaque properties of CHX are more effective than other antiseptic agents used in the mouthwash, due to its higher retentivity, and greater sustainability effect. It is often used after dental surgery and is prescribed after periodontal and implant procedures. Chlorhexidine proven in many clinical trials to be effective in reducing the formation of dental plaque and preventing gingivitis. Locally administered CHX chips are used as a long-term adjunct to oral hygiene in patients with periodontitis. Using CHX mouthwash can reduce plaque by 16–45% and gingivitis by 27–80%. These large differences in efficiency can be attributed to the frequency of use and mechanical oral hygiene procedures employed. Although CHX is not toxic, it has an unpleasant taste, alters taste sensation for up to 4 hours after rinsing, and produces brown staining on teeth, tongue, and restorations in long-term use.[38]

The addition of CHX to chewing gum is an attractive adjunct to conventional oral hygiene measures. In a clinical trial of elderly living in residential homes, subjects who chewed 2 pieces of CHX/xylitol gum for 15 minutes per day showed a significant ($p < 0.001$) decrease in plaque and gingival indices after 12 months compared to a control group.[39] Subjects were assigned to a 6-day plaque formation using chewing gum, with subjects chewing two pieces of CHX (5.0 mg CHX/piece), xylitol (0.8 g xylitol/piece), or sorbitol (1 g sorbitol/piece) each morning and evening after meals and one piece at noon. The study showed that chewing gum containing CHX significantly ($p < 0.01$) reduced the plaque value by 0.7 compared to 2.7 for the sorbitol and 1.7 for the xylitol, and the plaque value of xylitol products was significantly lower than that of sorbitol product ($p < 0.01$).[40] In another trial, the effectiveness of CHX was tested in 3 groups: Group 1 chewed 2 pieces of CHX chewing gum for 10 minutes twice a day, group 2 chewed placebo chewing gum in the same manner as group 1, while group 3 rinsed with 10 mL of 0.2% CHX mouthwash for 1 minute twice a day. At 8 weeks of the trial, plaque and gingival bleeding scores were significantly lower in the CHX gum group compared to the placebo gum group and similar to those in the mouthwash group. The trial also showed that the staining intensity induced by CHX chewing gum was significantly lower than that of the CHX rinse solution.[41] The use of eucalyptus extract chewing gum for 12 weeks to group with gingivitis resulted in a significant decrease in plaque accumulation, gingival index, bleeding on probing, and periodontal probing depth.[42]

Discussion

Saliva has several functions in maintaining oral and systemic health, with protection against dental caries and periodontal disease. The important function of saliva is to dilute and eliminate dietary sugars and acids, and to remove oral bacteria and potentially harmful substances from the mouth. Plus, it neutralizes the plaque pH after a sugar challenge by its buffering action; enhances the remineralization of early caries lesions, and maintains an environment saturated in calcium, phosphate, and. In stimulated saliva, supersaturation of Ca^{2+} and PO_4^{3-} plays an important role in the remineralization process. The production of acids by microorganisms in the dental plaque continues until the carbohydrate substrate is metabolized. The plaque's pH goes from acidic to normal resting level in 15–30 minutes, depending on saliva flow and the type of carbohydrate.

The rise of plaque pH is related to the saliva bicarbonate-phosphate-protein buffering system, which increases progressively in stimulated saliva. Increased numbers of and *Lactobacilli* are often associated with low salivation rates. The normal stimulated salivary flow rate averages 1.5–2.0 mL/min while the unstimulated salivary flow rate is approximately 0.3–0.4 mL/min. A diagnosis of hyposalivation is made when the stimulated salivary flow rate is ≤ 0.5–0.7 mL/min and the unstimulated salivary flow rate is ≤ 0.1 mL/min.[5,6] Increased saliva flow responds to gustatory (taste) and mechanical (chewing) stimuli, both of which are provided by chewing gum. It has been shown that on chewing flavored gum, the saliva flow rate initially increases from a resting value of 0.4–0.5 mL/min to approximately 5–6 mL/min and then declines as the flavor is lost from the gum, and the gum softens with chewing. After 15 minutes of chewing, the saliva flow rate slows to a level of around two to three times the resting rate at 60 minutes.[30, 34]

It is well recognized that products of low F concentrations and frequently used to deliver active F to enamel-plaque-saliva can significantly promote remineralization, F-chewing gum fit as an adjunct in caries prevention models. To date, the only chewing gums with the ADA seal are sugar-free.[1] They are sweetened by non-cariogenic sorbitol, xylitol, mannitol, or aspartame. The literature review provided evidence that chewing sugar-free gum stimulates saliva flow, restores the pH of plaque to its resting level, and reduces the increase in caries compared to no gum chewing. Although several studies have measured the release of F from chewing gum, there are few publications on the remineralization and caries-inhibitory effects of F-containing chewing gum. Consistent with our data, the peak of F released from chewing gum occurs after 5 minutes of chewing, and the AUC of salivary F concentration was 2 to 3 higher than that of non-chewing.[27,29,34] Bruun and Givskov[28] reported that chewing gum containing 0.25 mg F for 10 minutes increased salivary F concentrations to 11.7 and 15.3 ppm after 2 and 5 minutes, respectively, and then decreased to 3.9 ppm after 10 minutes. In a subsequent study, they recorded a peak of 15–25 ppm F for chewing gum containing 0.25 mg F. In their study, the peak F concentration at 5 minutes after chewing was 5.6–7.3 times higher than the 2.73 ppm F in our study when two sticks (0.23 mg F each) were chewed (Fig. 1). The AUC of the F concentration in saliva when chewing two gum sticks was 2.4 times that of chewing one stick, and more than 90% of the F content in the gum was released after 15 minutes of chewing.[35] Sjögren et al.[30] showed that prolonged chewing of F-gum enhanced plaque pH recovery after rinsing with a 10% sucrose solution, but had little effect on salivary F concentrations. Fluoride acquired by the plaque after gum chewing for 15 minutes was still present in the following 3 hours.[34] Contrary to the findings of Bruun and Givskov[27] that chewing gum provided significantly more F in saliva than the chewable F tablets, Sjögren et al.[29] showed that sucking F tablets had the same salivary stimulating effect and salivary F clearance pattern as F-chewing gum. *In-situ* tests have shown that chewing F-gum significantly promotes the remineralization of early enamel caries lesions, increased enamel microhardness, and increased F uptake and remineralization of early root surface lesions.[32–34] The effect of sugar-free chewing gum containing 50 µg F extracted from green tea was tested on subjects wearing intraoral appliances with attached blocks of demineralized tooth enamel, and chewing two pieces of gum for 20 minutes, twice a day for four weeks. Results showed that the peak salivary F concentration was 3.9 ppm and the F concentration in the remineralized area was four times higher than that for the placebo gum chewers.[43]

The safety of using chewing gum in children needs a comment. Bijella et al.[44] raised the risk of dental fluorosis in using the Brazilian Happydent-chewing gum containing 3.38 mg F/piece (as Na_2PO_3F) by saying "a single tablet of Happydent represents 39.4 and 16.4% of the maximum daily fluoride ingestion recommended for children aged 1 and 7 years old, respectively." Chewing gum has nothing to do with 1-year-olds. The authors refer to my article[35] in which two sticks of gum containing 0.23 mg F each were chewed and the pooled saliva swallowed had increased plasma F to a negligible level (Fig. 2). It should be noted that Na_2PO_3F contains 13% F^-, while NaF contains 45% F^-; therefore, the effect of Na_2PO_3F in increasing plasma F concentration is 3.5 times lower than that for the NaF. In their study, the salivary F released was 0.276 mg F, indicating that only 8.2% F^- of the 3.38 mg Na_2PO_3F was delivered. Also, gum use is uncommon in children under 7–8 years of age, which is the age at which enamel formation in the dentition is complete, and fluorosis does not occur regardless of how much F is ingested. According to the US National Institute of Health (NIH), typical daily F intakes in the United States from foods and beverages (including fluoridated drinking water) are 1.2–1.6 mg for infants and toddlers younger than 4 years, 2.0 – 2.2 mg for children aged 4–11 years, 2.4 mg for those aged 11–14 years, and 2.9 mg for adults.[45] Hence, the amount of ingested F reported by Bijella et al.[44] is 8.7 times lower than the typical daily intake. In accordance with our findings, a study by Oliveby[46] on 4 subjects used two pieces of chewing gum (Fluomin®) containing 0.5 mg F (as NaF) 10 times a day slightly raised the plasma F levels from 1 to 3 µmol/L (0.019 to 0.057 ppm); mirror those of water fluoridation from 1 to 1.5 ppm F and thus diminishing the fear of fluorosis. In this context, an intake of 250 mL (~1 tea cup) of tea leaves instilled in tap water containing 0.7 ppm will expose the body to 0.55 mg F [47], similar to chewing two sticks of gum containing 0.25 mg F (as NaF) each.[34] Evidence indicates that sugar-free fluoridated chewing gum is a safe and important oral and dental health supplement.

Conclusion

Chewing gum is an attractive low-concentration drug and chemical delivery vehicle with advantages such as ease of use, frequent topical application, and better human compliance. As a local delivery product, it is used to carry various dental and oral therapeutic agents such as F, CHX, hydrogen peroxide, sodium bicarbonate, mineral/metal salts, carbamide, etc. Adding sugar-free chewing gum to the regular home oral care of brushing with F toothpaste and interdental cleaning can reduce caries risk. A person should be strongly discouraged from chewing sugary gum, which has been proven to be cariogenic. Chewing gums containing F and CHX are important measures to prevent dental caries and gingivitis. The most important function of chewing gum is to strongly increase the volume and flow of saliva through mechanical action and flavors in the gum that stimulate saliva production. Saliva and its various constituents play an essential role in protecting teeth and oral health by removing fermentable sugar acids and food debris; increasing buffering capacity to neutralize plaque (biofilm) pH; decreasing numbers of pathogenic microbes, promoting remineralization of early caries lesions, and reduce enamel demineralization. Patients with hypo saliva/xerostomia may experience swallowing, chewing, and speech difficulties, mouth burning, bad breath, altered taste, dry oral mucosa, glossitis, cracked and peeling lips, oral candidiasis, dental caries, periodontal disease, and poor quality of life. The condition can be alleviated by chewing

sugar-free gum, saliva substitutes, and other palliative measures. It has been shown that most patients prefer chewing gum to artificial saliva and that chewing gum is better than artificial saliva on all efficacy measures. Clinical and research evidence indicates that therapeutic chewing gum has a place as an additional form of dental disease prevention that can be used in conjunction with traditional preventive methods.

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