Review Article

Combating white spot lesions via incorporation of remineralizing/ antibacterial additives into orthodontic adhesives: A review

Dana R. Mohammed[1,2], **Ali I. Ibrahim**[1,3*], **Sanjukta Deb**[3]

1 College of Dentistry, University of Baghdad, Baghdad, Iraq

2 Department of P.O.P., College of Dentistry, University of Basrah, Basrah, Iraq

3 Centre for Oral Clinical and Translational Sciences, Faculty of Dentistry, Oral and Craniofacial Sciences, King's College London, London, Uinted kingdom.

*Corresponding email: ali.ibrahim@kcl.ac.uk;

Received date: 15-06-2024

Accepted date: 18-08-2024

Published date: 15-06-2025

Article DOI

Abstract: Background: Orthodontic treatment with fixed appliances is frequently associated with difficulties in maintaining good oral hygiene and creation of plaque-retentive areas on tooth surfaces that are typically more prone to the development of caries; such drawbacks may result in white spot lesion (WSL) development that affects the esthetic outcome following bracket debonding. This review article focuses on orthodontic WSLs development, prevention, and remineralization potential via incorporating various remineralizing/ antibacterial additives into orthodontic adhesives. Results: Unbalanced enamel demineralization and remineralization processes, along with rapid alterations in the dental plaque bacterial ecology, particularly acidogenic bacteria, are the causes of the start and progression of a carious lesion. Without significantly compromising an adhesive mechanical performance, several antibacterial and remineralizing substances have been added to orthodontic adhesives in an effort to reduce bacterial colonization and promote remineralization. Conclusions: Antibacterial and/or remineralizing substances were utilized as additives in the creation of innovative orthodontic adhesive systems to address white spot lesions (WSLs) and improve the ability of enamel remineralization. Compared to adding only one agent, including multiple agents in an orthodontic adhesive system may have a greater impact on lowering enamel demineralization and improving enamel remineralization during orthodontic therapy.

Keywords: white spot lesion, enamel remineralization, orthodontic adhesive, bracket bonding, antibacterial agents.

Introduction

The prevalence of WSLs associated with orthodontic treatment was reported to range from 2-96% (1). Specifically, fixed orthodontic appliances represent a good environment for the development of WSLs as the surface irregularity of an orthodontic attachment impairs proper maintenance of oral hygiene resulting in plaque retention and accumulation of acidogenic bacteria mainly *S. mutans* and *Lactobacilli* (2). According to a previous study, 55% of orthodontically treated teeth developed at least one WSL, whereas 35% of treated patients were free of post-orthodontics WSL. The study also reported that the The prevalence of WSLs is 21% before fixed orthodontic treatment, and 65% of patients presented with WSLs following fixed orthodontic treatment (3).

The progression of WSL around fixed orthodontic attachments appears to be faster than in non-orthodontic patients, especially during the first 6 months of orthodontic treatment (4). A few years post orthodontic treatment, the more advanced WSLs become noticeably apparent, which could compromise the treatment's aesthetic results (5). Further to compromising the aesthetics, untreated WSLs can cause tooth cavitation necessitating additional restorative procedures; this raises a need for orthodontists to prevent the occurrence and development of WSLs during orthodontic treatment.

A number of studies have demonstrated the effect of using fluoride varnish against WSL during orthodontic treatment. Despite its low viscosity that facilitates its contact with the enamel surface and easy application to reduce demineralization, fluoride varnish requires recurrent applications every 4-6 weeks during orthodontic treatment. In addition to that varnishes function in the de- and remineralization process may be directly influenced by salivary flow clearance and lesion depth (6) (7). Therefore, Ibrahim et al in their studies adopted a novel paradigm of creating resistant enamel surfaces enriched with precipitated calcium-phosphate (CaP) ions, rather than the conventional concept that is dependent on CaP release. They incorporated β-tricalcium phosphate and monocalcium phosphate monohydrate powders into phosphoric acid solutions to develop novel orthodontic etchant pastes. In addition to encouraging safer enamel etching and bracket debonding, this novel technique of enhanced CaP re-precipitation can be used in conjunction with current initiatives to increase enamel resistance to demineralization during orthodontic treatment (8-10). Accordingly, the specific research question in this work was *'What is the effect of incorporating remineralizing antibacterial additives into orthodontic adhesives?'*

This review aimed to explore the possible strategies for prevention of WSLs, and to critically analyze the recent remineralizing/ antibacterial additives incorporated into orthodontic adhesive systems.

Methods of searching the literature

Up to January 2024, the peer-reviewed articles that matched the search terms were reviewed. Several databases including Google Scholar, Scopus, PubMed, and MEDLINE were used to gather research data. The following items were included in the search: white spot lesion, enamel acidic attack, enamel demineralization, enamel remineralization, remineralizing agents, antibacterial agents, orthodontic adhesive, bracket bonding, and fixed orthodontic treatment. After screening the abstracts of relevant studies to the search terms, full texts of those publications that fell within the scope of this review were retrieved and critically analyzed.

Results from literature

Development of white spot lesion

The minerals or inorganic components represent the bulk of tooth enamel by 96% whereas the remaining 4% is composed of 3% water and 1% organic component (11). According to Gorelick et al. (12), white spot lesion is defined as early carious lesion on enamel surface retained with bacterial plaque for a long period of time; the clinical white and chalky appearance of WSL is due to the subsurface mineral loss that overstated by rigorous drying. Fejerskov and Kidd (13) defined WSL as the first sign of a caries lesion on enamel that can be detected with a naked eye. Bishara and Ostby (14) described the WSL as a subsurface enamel porosity from carious demineralization that appears as a milky white opacity on smooth surfaces. Clinically, the WSL has a rough and porous surface compared with non-carious white spots that have smooth and shiny appearance. Heymann and Grauer (15) divided the term of WSL into three categories as following:

- Developmental enamel lesions such as fluorosis and enamel hypoplasia.
- Localized areas of demineralization/caries in non-orthodontic patients.
- Localized areas of demineralization/caries associated with orthodontic appliances.

The initiation and progress of a carious lesion occur because of imbalance between natural enamel demineralization and remineralization processes, and rapid changes in the bacterial flora of the dental plaque, specifically acidogenic bacteria. When a sufficient fermentable carbohydrates supply is provided, the bacterial acid by-products are produced, lowering the plaque pH below that required for remineralization, so that demineralization takes place and is visualized as a WSL (13) (14) (16).

White spot lesion and orthodontic treatment

Within 14 days of undisturbed accumulated plaque, the changes in the enamel surface appear to be visible clinically via thorough drying. On the following 4 weeks that represent the interval period between orthodontic visits, porosity of the enamel surface is increased, and enamel changes might be visualized clinically without air drying [(12)]. Recalcification can occur within the WSL with time, but its opacity may remain and lead to a remarkably less aesthetic appearance [(17)], Figure 1.

The cervical area of the buccal side of teeth around orthodontic brackets is regarded as the commonest site for WSL development, especially for the maxillary lateral incisors, with the least common site is maxillary posterior segment [(17)]. Julien et al. [(18)] reported that the rate of occurrence of WSLs was 2.5 times more in the maxillary arch than in the mandibular arch, and it usually takes place on the maxillary lateral, maxillary canine, and mandibular canine.

Figure Error! No text of specified style in document.**:** WSLs on enamel surface related to fixed orthodontic appliance.

Prevention of white spot lesion

According to Featherstone [(19)], three factors are essential for demineralization to occur: fermentable carbohydrate, acidogenic bacteria, and reduced salivary flow. Whereas the three factors essential for enamel remineralization are fluoride, antimicrobial agents, and salivary flow. Accordingly, there are two modalities for prevention of WSLs (Figure 2) as described below.

A. Prevention of demineralization (loss of minerals from enamel)

1- Oral hygiene control and reducing the amount of acidogenic plaque: it is obvious that maintenance of good oral hygiene is more important in individuals treated with orthodontic appliance than non-treated ones. Improving oral hygiene should be started by education and motivation of the patient as a prophylactic step prior to orthodontic treatment, with periodic observation of oral hygiene during treatment [(20-22)].

2- Dietary control (Reducing the frequent consumption of sugar): the oral cavity is exposed to cariogenic carbohydrates. A high-sugar diet promotes the metabolism of cariogenic bacteria, which settle as the main strain in the biofilm covering the dental surfaces. A cavitated lesion develops and results in damaged tooth surface if it is not halted or controlled by proper oral hygein measures [(23)] [(24)].

3- Sealing and protecting the enamel: new modalities for prevention of enamel demineralization without reliance on patient cooperation, especially for young patients, have been introduced. Orthodontic sealants or primers have been proposed to prevent mineral loss from enamel by adding these agents onto the tooth surface during orthodontic bonding, yet their use was associated with drawbacks related to the loss of the sealant material; i.e. short-term effectiveness [7].

B. Promoting remineralization (uptake of minerals into the enamel)

1. Fluoride: Fluoride has been shown to have a beneficial function in preventing WSL when it is used in mouthwashes, toothpastes, gels, varnishes, and other products [20]. According to Mitchell [1], fluoride aids in reduction of caries occurrence via the following mechanisms:

- Acts as a catalyst in the formation of high-quality hydroxyapatite.
- Aids in remineralisation during pH fluctuations.
- Inhibits glycolysis of plaque bacteria.

➢ Toothpastes, mouthwashes, and varnish: remineralization could be induced by using high fluoride concentration toothpaste (5000 ppm) [25] [26]; whereas the frequency of WSLs is decreased when toothpaste with more than 1000 ppm fluoride is used at home [27]. Regarding the fluoride mouthwashes, the efficacy of mouthwashes may be limited by bonded enamel surfaces, despite the fact that using a mouthwash containing 230 to 250 ppm fluoride and 0.05% NaF per day was advised to prevent enamel demineralization during fixed orthodontic treatment [28] [29].

Fluoride varnishes adhere to the tooth surface in a thin layer for longer periods of time (12 hours or more) and prevent fluoride from being immediately lost after application, they serve as slow-releasing reservoirs of fluoride that reduce the likelihood of acute toxicity. Originally, varnishes were developed to increase the amount of time that fluoride and dental enamel come into contact, which requires two to four applications annually. This regimen demonstrated efficacy in reducing the occurrence of caries in both permanent and deciduous teeth, yet it requires frequent visits and applications [30].

➢ Orthodontic elastics: introducing elastics with a low-dose fluoride release over a long period of time is a desired requirement to increase concentration of fluorapatite in enamel and provide caries resistance [31]. However, elastics' physical characteristics may be impacted by adding fluoride, which resulted in deterioration more quickly in the oral cavity. At day 1 of elastomeric placement, 35% of total fluoride released out, and at the end of the 1st month about 85% of total fluoride released out [32].

➢ Bonding materials: fluoride releasing compounds such as stannous fluoride, fluoroaluminosilicate glasses, and yttrium fluoride were incorporated into orthodontic adhesives. Remarkably, numerous investigations have documented that fluoride-releasing restorative materials increased the acid resistance of the resin-enamel and resin-dentin interfaces, consequently exhibiting a cariostatic effect. However, the short-term release was again a major shortcoming [33].

➢ Diet: the use of fluoridated water, milk, and salt represented a traditional way to prevent dental caries. However, there is weak evidence to support their use due to their low efficiency in reduction of dental caries [34].

2. Sugar-free chewing gum: it has been used to increase salivary flow and pH of saliva in order to induce an anti-caries effect and increase production of stimulated saliva that has higher calcium and phosphate concentrations than non-stimulated saliva, hence enhancing the remineralization effect [35]. It was reported that the daily use of sugar-free chewing gum may reduce the severity and lesion depth of WSLs, yet this depends on the frequent intake and requires patient compliance [36]. Moreover, frequent chewing of gum may interfere with the survival of bonded orthodontic attachments/brackets.

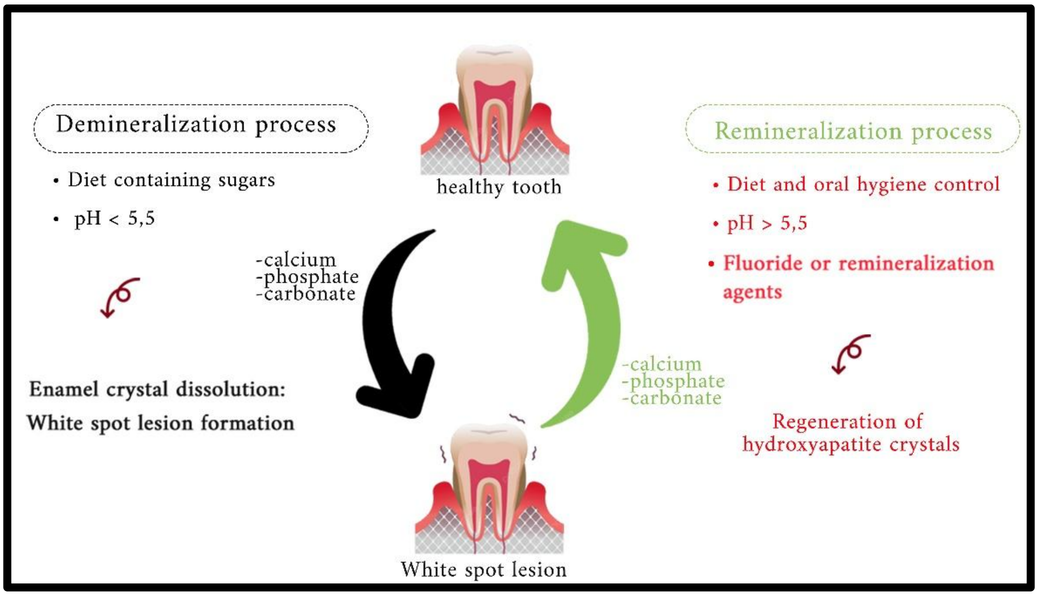

Figure 2: Mechanism of teeth demineralization and remineralization.

Remineralizing and antibacterial additives to orthodontic adhesives

The addition of various antibacterial/remineralizing materials to orthodontic adhesives has been attempted to decrease the bacterial colonization and enhance remineralization without adversely affecting the mechanical performance of the adhesives (37). The following materials represent the most commonly used as remineralizing and\or antibacterial additives to orthodontic adhesives

1. Fluoride

Inhibition of demineralization and enhancing remineralization of small, decalcified lesions could be achieved by inclusion of fluoride into enamel structure and formation of fluorapatite crystals, which improve the enamel resistance to the acidic attacks by oral bacteria. Initial discharge of fluoride occurred in the first day of using fluorinated orthodontic adhesives, followed by gradual declining throughout the next three weeks. Significant reduction of demineralization was observed when these adhesives were used (38) (39).

2. Silver nanoparticles

Several synthetic and natural processes have been devised to generate silver nanoparticles (AgNPs) via biological techniques favored to prevent toxicity during synthesis, by utilizing microorganisms such as fungi, bacteria, and plants such as moringa oleifera leaf extract, thus, avoid synthesizing harmful compounds (40) (41). Previous studies demonstrated that addition of AgNPs to orthodontic resins exhibited a significant antibacterial impact that prevented *S. mutans* growth in in vitro models (42) (43). Orthodontic resin containing 0.5% and 1% AgNPs was shown to have significant antibacterial activity against *S. mutans* and *L. acidophilus*, and it also inhibited the development of WSL (44).

3. Copper Oxide Nanoparticles

Compared to Ag, Copper Oxide (CuO) is less expensive, simpler to combine with polymers, and has more stable chemical and physical characteristics. It was suggested that CuO nanoparticles could combat a variety of bacterial species, with less bactericidal action than silver (45). However, Shamaa et al (46) compared the incorporation of silver and copper oxide nanoparticles into orthodontic adhesives, and found that either AgNPs or CuONPs exhibited the same antibacterial efficacy against *S. mutans* and had no adverse effects on adhesive mechanical properties. Gutiérrez et al (47) added a combination of copper NPs and zinc oxide NPs to two universal adhesive systems, they demonstrated that this addition was effective with no noticeable biological risks, and enhanced the adhesive system antibacterial capabilities as well as improved and stabilized resin-dentin interface.

4. Calcium phosphates

Calcium and phosphate are essential for the maintenance of strong, healthy teeth, and the amounts of these minerals in saliva and plaque have a significant impact on the processes of tooth demineralization and remineralization. Because of their resemblance to natural enamel, calcium phosphates have been discovered as viable biomimetic alternatives. Calcium phosphate is thought to work by entering the micropores in early caries lesions, where it attracts a lot of calcium and phosphate ions from the oral fluids into the lesion acting as crystal nuclei in the remineralization process and facilitating natural remineralization processes (48). A number of calcium phosphate phases has been used for enamel remineralization as described below.

a. Casein phosphopeptide-amorphous calcium phosphate complexes (CPP-ACP): In the early stages of WSL, remineralizing agents including CPP-ACP may be employed as non-invasive therapies. It is a milk-derived product that acts as a reservoir for calcium and phosphate, facilitating their binding to enamel surface to promote remineralization (49). CPP-ACP has anticariogenic property and aids in reduction of *S. mutans* through incorporation in the dental pellicle and inhibition of bacterial adhesion to the dental plaque. Demineralized enamel has a different refractive index from that of sound enamel surface, and CPP-ACP has the ability to reduce the difference in the refractive indices and fills the pores of subsurface enamel, hence improving the aesthetic and translucent appearance of WSLs (50). Additionally, the liberation of calcium and phosphate from a CPP-ACP paste resulted in the formation of nano-complexes in the dental biofilm covering the white spot lesions and provided increased enamel resistance against future acidic impacts. However, a single application of paste did not result in a discernible remineralization of the white spot lesions, despite the specimens were kept in a remineralization solution for seven days following the application of CPP-ACP paste and were not exposed to any additional acidic challenges. Hence, multiple reapplications were recommended, up to four weeks, in order to significantly remineralize the demineralized enamel (51) (52).

b. Hydroxyapatite: The main benefits of hydroxyapatite (HA) nanoparticles are their bioactivity, biocompatibility, and highest similarity to the mineral structure of teeth. In fact, the particles of 20 nm size resemble dental apatite in morphology and crystal structure, and have similar properties to enamel's natural building components. Calcium hydroxyapatite nanoparticles can effectively fill the micropores seen in enamel by releasing inorganic ions and exhibit a significant attraction for demineralized enamel surfaces (53). Bossù et al. demonstrated via in vitro and in vivo studies the coating effect of micro-structured hydroxyapatite nanoparticles that could restore the enamel's structure and morphology by creating a biomimetic film that mimics the biologic hydroxyapatite of the enamel. Furthermore, due to the chemical connections between the enamel's natural and manufactured crystals, the newly formed biomimetic film exhibited brushing resistance. In 2023, Rahmanpanah et al. conducted an in vitro study via inclusion of varying percentages of nano-hydroxyapatite particles in an orthodontic adhesive and reported that the mineral content and microhardness of the neighboring enamel can be raised by adding hydroxyapatite nanoparticles to orthodontic composite. The same results were concluded via Raheem and Jehad in vitro study in 2023, in which the potential of nano-hydroxyapatite to remineralize early enamel caries lesions under dynamic pH-cycling settings were tested. The shear bond strength, however, tended to decrease as the percentage of nanoparticles increased (54-56).

c. β-tricalcium Phosphate (β-TCP): There are two known forms of tricalcium phosphates $Ca_3(PO_4)_2$, none of which can be found in nature in its pure form. β-TCP is stable at room temperature, unlike α-tricalcium phosphate that can only exist at high temperatures (over 1125 °C). β-TCP is a bioactive source of mineralizing components and an attractive CaP system because of its low solubility in comparison to other calcium salts and minerals (56). According to a prior study by Tavassoli-Hojjati et al. [57], the material's ability for remineralization can be enhanced by adding 1%–5% of β-TCP nanoparticles. Moreover, Ibrahim et al [8] [9] developed a new strategy for safer enamel conditioning via the incorporation of β-TCP into an etchant paste, as CaP re-precipitation was encouraged to increase enamel resistance to demineralization. Enamel remineralization takes place in response to an increase in the concentration of calcium in the saliva that occurs when using β-TCP as it is soluble at pH < 6, the calcium rise follows acidic attacks and an acidic plaque pH [8] [10] [58]. β-TCP is considered one of the mainly used CaP as most CaP additions require an acidic environment to release calcium ions, yet β-TCP can achieve the optimal calcium ion release effect even in a pH-neutral setting.

d. Calcium Glycerophosphate (CGP): CGP is the salt of glycerophosphoric acid, usually utilized as a dietary supplement and ingredient in food. It was utilized as a dietary supplement in the initial research conducted by Bowen in 1972 to assess the cariostatic effect of this organic calcium phosphate. It is believed that CGP promotes plaque pH buffering by raising the levels of calcium and phosphorus in plaque and in the enamel hydroxyapatite, in addition to the antimicrobial properties. The addition of CGP to a highly cariogenic and carbohydrate diet resulted in a significant drop in caries during experiments conducted on rats, but there was no effect observed when CGP was added to the animals' drinking water. More enamel remineralization occurred when CGP was added to SMFP (sodium Mono-fluorophosphate) mouth rinse than when fluoride mouth rinse was used alone. According to previous studies, the addition of CGP enhanced remineralization without amplifying the effect of fluoride concentration [59] [60]. However, CGP should be used frequently at high concentrations to obtain antibacterial effects, unlike β-TCP that must be used at a concentration less than 1% when used in conjunction with fluoride due to the potential adverse interactions [61].

5. Bioactive glass

There are several types of bioactive glasses (BAG), including silicate- and phosphate-based glasses. It is well recognized that BAG promotes bone regrowth and repairs bone defects, and a comparable response was seen in the tooth [62]. Mineralizing agents from saliva, the phosphate and calcium ions found in the bioactive glass can both initiate the mineralizing process. BAG NPs exhibit superior remineralization and slower carious lesion progression in comparison to traditional BAGs owing to their larger surface areas and higher Ca/P ratios [63]. Several studies investigated the effects of incorporating bioactive glass with other materials such as Graphene oxide, fluoride, and strontium into orthodontic adhesives. Further to the remineralization capability of bioactive glass, the addition of antimicrobial ions such as strontium resulted in strong inhibitory effect against *S. mutans.* Moreover, fluoride in bioactive glass resulted in fluorapatite on the surface of the tooth, increasing resistance to acid breakdown. Therefore, the addition of such materials to bioactive glass may improve bonding capabilities and reduce enamel demineralization during orthodontic treatment [64-66].

Discussion

White spot lesions are indicators of demineralization behind a layer of undamaged, highly mineralized enamel. Demineralization is a process that results in dissolution of hydroxyapatite in an acidic environment, which causes mineral loss from the enamel and formation of porosities. In many cases, especially for individuals with fixed orthodontic appliances, maintaining good hygiene during orthodontic treatment can be quite challenging. It is now known that fixed orthodontic appliances have an innate tendency to encourage the retention and build-up of bacterial plaque, which impedes the regular cleaning procedure. This indicates a higher risk of developing caries and the related periodontal concerns [67]. Several studies suggested the use of electric toothbrushes for mechanical removal of plaque in orthodontic patients and non-treated individuals [68] [69]. Others suggested the use of chlorhexidine mouth rinse, toothpaste, and varnish for chemical control of dental plaque by reducing the gingivitis and numbers of *S. mutans* up to 4 weeks [70]. Despite the fact that patients had received instructions on proper oral hygiene and that mouthwash and tooth brushing techniques were taught to the orthodontic patients, younger patients ignored these instructions. Therefore, it is imperative to introduce a strategy to prevent

WSLs that is independent on patient cooperation. Special considerations were given to prevent the WSLs development, enamel remineralization process could be carried out naturally by minerals present in saliva but this procedure may only interfere with WSLs superficial layer and affect esthetic result, for the treatment of deeper lesions and better aesthetics, remineralizing chemicals are necessary, such as fluoride, casein phosphopeptideamorphous calcium phosphate (CPP-ACP), bioactive glass.

Although the prevention of enamel demineralization could be assisted by using fluoride, there is a weak therapeutic effect and insufficient evidence concerning fluoridated toothpaste and mouthwashes effectiveness against demineralization during orthodontic treatment [62]. Hence, it is advisable to use alternative fluoride sources such as fluoride varnish that requires low patient compliance, merely attendance at the dental office. Varnish application of a high fluoride concentration (wet 7,700 ppm; dry 30,000 ppm) resulted in 44.3% decrease in enamel demineralization. Thus, fluoride varnish can be considered as an interesting tool against enamel demineralization in non-compliant patients and those with physical disability to brushing, but a single application of fluoride varnish before starting orthodontic treatment did not offer any additional preventive benefit of WSLs prevention over using fluoridated toothpaste and good dental hygiene maintenance [20]. As the varnish gets worn down in a matter of days by brushing and oral functions, the application of fluoride varnishes every six weeks around bracket bases during orthodontic treatment is required to prevent development of WSLs [71]; hence the cost and frequent visits to the dental clinic need to be taken into consideration.

WSLs can be avoided by following proper oral hygiene, and patient compliance is primarily needed for effective prevention. It has been noted that there is a strong correlation between the development of WSLs and insufficient compliance with homecare preventive measures. Many studies were conducted to introduce compliance-free approaches for WSLs prevention that concentrated on fluoride-releasing adhesives, sealants, and primers on the premise of providing continuous fluoride release during orthodontic treatment. However, the mechanical properties of the resin-based adhesives were weakened by the addition of fluoride, and these adhesives encountered a dramatic decline in fluoride release in a short time and did not offer a considerable inhibition of demineralization [27] [72] [73].

The use of metallic nanoparticles has been suggested as a valuable tool against bacterial biofilm development. The incorporation of silver nanoparticles into orthodontic adhesives was investigated by Ahn et al. [74], who reported that these nanoparticles were able to penetrate the saliva coating, inhibit bacterial growth and prevent WSLs around orthodontic brackets without adversely affecting the adhesive mechanical properties. Argueta-Figueroa et al. [75] used copper nanoparticles with an orthodontic adhesive, they noticed an antibacterial activity with a significant increase in the shear bond strength and adhesive remnant index. Owing to their size and high surface-volume ratio, the nanoparticles interact with the bacteria's membrane, which contributes to their antibacterial efficacy in addition to the release of metal ions [76].

It has been proposed that CPP-ACP can have a favorable additive effect to fluoride in inhibition of demineralization, and a combination of fluoride and CPP-ACP produced the best WSLs remineralization. CPP-ACP acts as a calcium and phosphate reservoir and the suggested anticariogenic mechanism of CPP-ACP is related to the integration of the nanocomplexes into dental plaque and onto the tooth surface. According to Anggani et al. [77] and Aref and Alrasheed [78], the regular daily use of CPP-ACP for a short period of time could enhance the aesthetic appearance of WSLs. However, due to the agent's limited ability to penetrate the outer layer of enamel, this minimally invasive method does not address the aesthetic issue in advanced lesions and may leave a discolored area untreated [79].

Acidogenic bacteria found in biofilms in the oral environment produce acids that drop the pH, demineralize tooth tissues (losing Ca^{2+} and PO_4^{3-}), and raise the possibility of developing caries; this necessitates the use of "smart particles" that can release large amounts of Ca^{2+} and PO_4^{3-} when the oral pH falls below the crucial 5.5 level. During the remineralization process, Ca^{2+} and PO_4^{3-} diffuse across interprismatic gaps and transform into hydroxyapatite crystals. Since the latter crystals have lowest solubility of all calcium phosphate phases, quick ion release and ability to produce active oxygen species, the nano-sized hydroxyapatite particles can exhibit the best antibacterial effects (80). The low solubility of hydroxyapatite crystals and the bulk of their crystallites led to the mineral deposition on the demineralized enamel surfaces and interfered with demineralization process. However, such mineral deposition may have a weakening effect on bond strength as it impedes the diffusion of adhesive monomers into the surface micropores that are formed upon enamel etching. Therefore, Garma and Ibrahim (81) (82) and Kadhim et al. (83) (84) developed novel hydroxyapatite-based orthodontic bonding systems that can simultaneously precipitate calcium-phosphate (CaP) salts for remineralization and condition the enamel surface without sacrificing bond strengths or inducing enamel damage.

The conditions created by the adherence of orthodontic brackets are conducive to bacterial colonization, which can cause demineralization of the enamel and WSL. Amongst biomaterials, Bioactive glass was brought to the dental field because of the remineralization action. BAG 45S5 and S53P4 have been approved by the US Food and Drug Administration (FDA) for use in clinical situations where antimicrobial activity is sought. In comparison to topical fluoride and CPP-ACP, Bioactive glasses have the potential to promote and improve the remineralization of enamel since they display a constant release of calcium rather than an initial calcium burst (85) (86).

BAG is composed of elements that are naturally present in the human body, including calcium, phosphorous, sodium, and silica (calcium sodium phosphosilicate). BAG particles remineralize dental surfaces when they come in contact with saliva or water, forming hydroxycarbonate apatite (HCA) layer on their surfaces and releasing sodium, calcium, and phosphorus ions into the saliva (87). Ion substitutions are frequently encountered in BAGs, and all play a part in the final characteristics of dental composite. Addition of fluoride to the BAG depends on phosphate content (P_2O_5) such that in high phosphate BAG, fluoroapatite can be formed in less than six hours, which exhibits greater acid resistance, lower degradability, and is more stable chemically and thermodynamically than HCA. In contrast, there is a delay in apatite layer formation with low phosphate BAG (88). However, Nam et al. (89) added a mixture of fluorinated bioactive glass to orthodontic adhesive, their results showed that the antibacterial activity of FBAG aids in inhibiting demineralization surrounding the orthodontic appliance, which is brought on by the lactic acid that plaque bacteria creates.

Bioactive glass degradation, apatite formation, and ion release were inhibited by the presence of MgO and ZnO in a way that high concentrations of Mg and Zn ions can result in delayed glass dissolution, and prevent the production of apatite layers. The substitution of zinc for calcium resulted in a significant decrease in ion release at physiological pH, which completely prevented the precipitation of apatite due to insufficient calcium and phosphate ions. In contrast, because of its stronger field, magnesium behaved similarly to calcium, lowering ion release slightly. However, magnesium ions inhibited the nucleation and crystallization of apatite, resulting in a considerable reduction in apatite formation (90). Although the addition of strontium to BAG improves bonding capabilities, when adding fluoride and strontium to BAG, the acid produced by cariogenic bacteria cannot dissolve hydroxyapatite as easily and in the event of precipitate formation, strontium can take the role of calcium, and it works in concert with fluoride to prevent caries. Therefore, Strontium can stop caries lesions because of its ability to remineralize dental hard tissues (66) (91) (92).

As the surface of the BAG plays a significant influence in its bioactive applications, surface modification techniques are constantly being researched to improve its biocompatibility and bioactivity. Graphene oxide (GO) is one of carbon nanomaterials that have drawn a lot of study attention to alter the surface of biomaterials because of its exceptional mechanical properties, high strength, huge surface area, and strong cytocompatibility. Additionally, GO can promote hydroxyapatite mineralization and osteogenic differentiation, which can increase calcium fixation. In (2018) Lee et al. added a mixture of Graphene oxide with bioactive glass to orthodontic adhesive, and in (2019) Nam et al. added a mixture of fluorinated graphite and bioactive glass to orthodontic adhesive. Both concluded that addition of those mixtures is effective in reducing enamel demineralization during orthodontic treatment; however, fluorinated graphite bioactive glass mixture was associated with a reduction in shear bond strength due to grey color and low polymerization. These results were evidenced by a systematic review of Alamri et al. (65) (89) (93).

Conclusion

Two strategies have been implemented to avoid white spot lesions (WSLs) during orthodontic treatment. These strategies involve either inhibiting the loss of minerals from the enamel or promoting the absorption of minerals into the enamel. Antibacterial and/or remineralizing substances have been utilized as additives in the creation of new orthodontic adhesive systems to address white spot lesions (WSLs) and improve the ability of enamel to undergo remineralization. Compared to adding only one agent, including multiple agents in an orthodontic adhesive system may have a greater impact on lowering enamel demineralization and improving enamel remineralization during orthodontic therapy. Bioactive glass is a promising material in field of enamel remineralization, further researches and trials need to be accomplished to address their effectiveness.

Conflict of interest

The authors have no conflicts of interest to declare.

Author contributions

All authors participated in the study design, data collection, result interpretation, drafting of the manuscript, and revising and finalizing the manuscript.

Acknowledgement and funding

No grant or financial support was received from any governmental or private sector for this study

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مكافحة آفات البقع البيضاء من خلال دمج إضافات إعادة التمعدن / المضادة للبكتيريا في المواد اللاصقة لتقويم الأسنان: مراجعة

دانة رفعت محمد, علي إسماعيل إبراهيم, سانجكتا ديب

المستخلص:
يرتبط علاج تقويم الأسنان بالأجهزة الثابتة في كثير من الأحيان بصعوبات في الحفاظ على نظافة الفم وإنشاء مناطق تحتفظ بالبلاك على أسطح الأسنان والتي عادة ما تكون أكثر عرضة لتطور التسوس؛ قد تؤدي مثل هذه العيوب إلى تطور آفة البقع البيضاء
(WSL)التي تؤثر على النتيجة الجمالية بعد فك الأقواس التقويمية. تركز مقالة المراجعة هذه على تطور آفة البقع البيضاء المصاحبة لتقويم الأسنان والوقاية منها وإمكانات إعادة التمعدن من خلال دمج إضافات إعادة التمعدن / المضادة للبكتيريا المختلفة في المواد اللاصقة لتقويم الأسنان. تم استخدام الموارد الإلكترونية مثل Google Scholar و Scopus PubMed و MEDLINE للبحث عن مصادر معلومات حول آفات البقع البيضاء .إن عمليات إزالة المعادن وإعادة التمعدن غير المتوازنة في مينا الأسنان، إلى جانب التغيرات السريعة في البيئة البكتيرية وخاصة البكتيريا الحمضية، هي أسباب بداية وتطور الآفة تمت إضافة العديد من المواد المضادة للبكتيريا وإعادة التمعدن إلى المواد اللاصقة لتقويم الأسنان في محاولة لتقليل الاستعمار البكتيري وتعزيز إعادة التمعدن في العديد من الدراسات السابقة دون المساس بشكل كبير بالأداء الميكانيكي لمواد التقويم اللاصقة. تمثل WSLs أحد الآثار الجانبية النموذجية للعلاج بأجهزة تقويم الأسنان الثابتة خاصة في حالة القواطع الجانبية العلوية. في الآونة الأخيرة, تم استخدام المواد الكيميائية المضادة للبكتيريا و / أو إعادة التمعدن كإضافات في تطوير أنظمة ومواد لاصقة لتقويم الأسنان في محاولة لمكافحة WSLs وتعظيم إمكانات إعادة تمعدن المينا.