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Original Article

Mitigating White Spot Lesions During Fixed Orthodontic Treatment: A Comprehensive Literature Review

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Abstract

The purpose of this review is to examine current literature concerning methods to prevent white spot lesions (WSLs) that arise during fixed orthodontic treatment. These lesions, caused by enamel demineralization, create both functional and cosmetic problems. This paper assesses the efficacy of different preventive strategies designed to minimize the risk of WSL development during orthodontic care. A structured search was carried out using MeSH terms including "white spot," "fixed orthodontic treatment," "CPP-ACP," "topical fluoride," and "demineralized lesion," combined with the Boolean operator *AND*. Databases such as PubMed, EMBASE, Scopus, and OpenGrey were explored for studies published from January 2014 to September 2024. Only studies that evaluated preventive interventions for patients receiving fixed orthodontics were included. Out of 41 initially screened papers, 17 were retained for analysis based on relevance and methodological quality. Multiple preventive options were identified. Topical fluoride, particularly in high-dose varnish form, consistently lowered the prevalence of WSLs, with several studies favoring varnish compared to other delivery systems. Casein phosphopeptide–amorphous calcium phosphate (CPP-ACP) and CPP-ACPF products also showed remineralization potential, especially when paired with fluoride toothpaste. The use of high-fluoride dentifrice and acidulated phosphate fluoride rinses was effective in reducing lesion incidence, highlighting the critical role of patient compliance with daily hygiene. Periodically repeated professional fluoride applications enhanced preventive success. Addressing WSLs is essential to preserve both function and appearance during orthodontic therapy. The combined use of fluoride-based methods with CPP formulations appears particularly advantageous. Nevertheless, patient motivation and adherence to oral hygiene remain key determinants of outcomes. More research is required to evaluate the long-term benefits of these interventions and to explore novel approaches for WSL control.

Key words: White spot lesions, Orthodontics, Enamel demineralization, Preventive interventions

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Introduction

Dental caries is a widespread, chronic infectious disease caused by bacterial activity, affecting a large share of the population, especially children and adults of school age. It develops when plaque bacteria metabolize sugars, leading to acid production, enamel demineralization, and eventual cavity formation. Contributing factors include frequent sugar intake, insufficient oral

hygiene, and individual host susceptibility [1]. White spot lesions (WSLs) represent the earliest visible stage of caries, marked by enamel demineralization without cavitation, producing a chalk-like surface. While remineralization can sometimes reverse the process, ongoing mineral loss may cause permanent cavities. Even when stabilized, WSLs often leave cosmetic traces [2].

These lesions are highly prevalent among orthodontic patients, often developing within weeks after appliance placement, especially around brackets or beneath molar bands. Fixed appliances make plaque control more difficult, leading to increased risk of WSLs, which can undermine treatment outcomes and aesthetic goals [3]. Orthodontic brackets, a critical component of fixed appliances, significantly contribute to demineralization because their design complicates effective cleaning and creates retention sites for plaque accumulation [4]. Materials with rougher surfaces encourage stronger bacterial attachment and protect biofilm against mechanical disruption. Likewise, materials with high surface free energy enhance bacterial binding and plaque retention. Bracket design—size and shape—also affects colonization; thus, smaller and simpler brackets are recommended to minimize biofilm accumulation [5].

For this reason, patient education is essential prior to treatment, emphasizing proper hygiene practices and the added difficulty of maintaining cleanliness with orthodontic appliances [6]. Individuals undergoing orthodontic care face heightened risk of developing WSLs, making preventive protocols such as fluoride application and remineralizing agents necessary. Patients with malocclusion often experience challenges in cleaning difficult-to-access areas, facilitating plaque buildup. WSLs typically appear on upper lateral incisors and canines close to brackets within the first month of treatment, although the progression to cavitation generally requires at least six months [7].

Key risk factors for tooth decay include frequent sugar consumption, inadequate brushing, insufficient fluoride protection, and irregular dental care. Children and teenagers are the groups most affected. In addition, social and demographic aspects such as income, education, occupation, gender, age, and ethnicity play a role in determining caries susceptibility. Preventive behaviors—like using fluoride toothpaste twice daily and attending regular dental checkups—remain fundamental in reducing risk [8]. Fixed orthodontic appliances not only create discomfort but also promote plaque retention. Over long treatment durations, this can result in the development of white spot lesions, which compromise dental appearance even after successful alignment [9].

Caries prevention strategies include the use of systemic fluoride supplements, fluoridated community water, and daily use of fluoride-containing toothpaste. The recommended concentration for drinking water is approximately 1 ppm, which provides anticariogenic benefits while minimizing fluorosis risk. For patients affected by enamel anomalies such as molar incisor hypomineralization (MIH), amelogenesis imperfecta, or fluorosis, fixed appliances may be less suitable. These conditions lead to reduced adhesion, fragile enamel, and a greater likelihood of plaque accumulation. Porous enamel surfaces, together with the difficulty of cleaning around brackets, amplify the problem [10].

CPP-ACP (Casein Phosphopeptide-Amorphous Calcium Phosphate) supplies calcium and phosphate ions directly to weakened areas of enamel. By doing so, it assists in repairing early enamel changes like white spot lesions and shields the surface from acid challenges. Widely incorporated into oral care products, this compound supports enamel strengthening and decay prevention [11]. Fluoride, by contrast, reinforces enamel by substituting hydroxide ions with fluoride ions, producing fluorapatite, a crystal more acid-resistant. This mineral replacement process restores enamel hardness and improves resistance to caries [12].

Objective of the study: to analyze the available scientific evidence and determine how effective different preventive interventions are in lowering the occurrence of white spot lesions in patients treated with fixed orthodontic appliances.

Materials and Methods

This investigation was carried out as a structured review of the literature, concentrating on research that examined active agents or preventive protocols intended to limit the development of white spot lesions during orthodontic therapy with fixed appliances.

Two reviewers (RGP and FSL) independently assessed records, applying the following **inclusion criteria**: clinical studies, randomized controlled trials, or systematic reviews; research involving patients under fixed orthodontic therapy; and studies specifically addressing WSL prevention in orthodontic patients.

Exclusion criteria were: (1) investigations of WSL management after orthodontic treatment; (2) research on lesions unrelated to orthodontics; (3) laboratory-only experiments; (4) animal-based studies; and (5) narrative reviews, systematic reviews, or meta-analyses.

The search terms included Medical Subject Headings (MeSH) such as “Dental Caries,” “Orthodontic Appliances,” “Tooth Demineralization,” “Fluorides,” and “Caseins,” supplemented by free-text keywords like “White Spot Lesions,” “Fixed Orthodontic Treatment,” “CPP-ACP,” and “Topical Fluoride.” Databases searched were PubMed, EMBASE, Scopus, and OpenGrey. The time frame covered January 2014 through September 2024 (Appendix A). The initial screening was conducted on June 16, 2024, and full-text evaluations were completed between June and September 2024.

From 41 potentially relevant publications, screening of titles and abstracts was performed. After full-text assessment, 17 studies met the criteria for inclusion. These comprised randomized trials, in vitro and in vivo experiments, systematic reviews, and other review articles **(Figure 1)**.

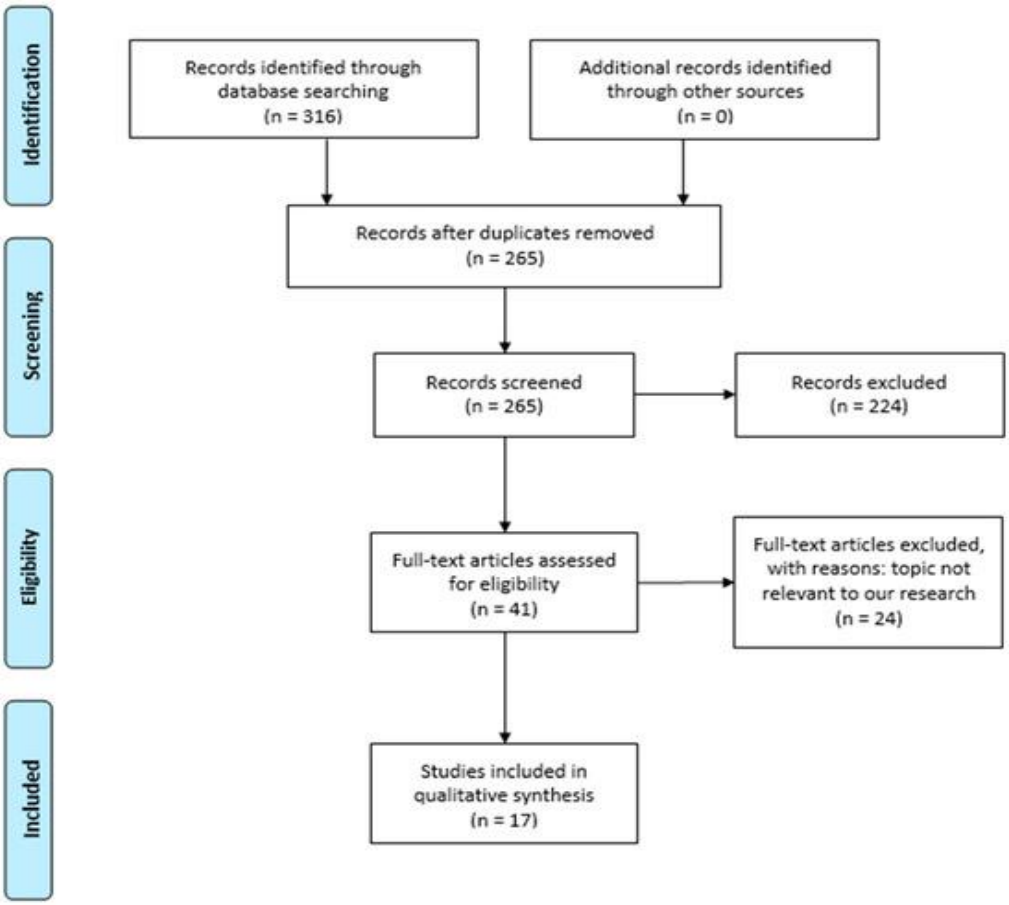

Figure 1. PRISMA 2009 flow diagram

Results

A total of 41 potentially relevant publications were identified through database searches. After reviewing the full texts and applying the inclusion and exclusion standards, 17 articles were selected. These comprised randomized controlled clinical trials, systematic reviews, meta-analyses, in vivo experiments, and in vitro investigations. **Table 1** presents a structured overview of the chosen works from internatiOnal literature. Arranged in columns, the table outlines the article title (according to eligibility criteria), author(s), publication year, study objective, methodology, and main conclusions. The included studies consist of systematic reviews, narrative reviews, in vitro and in vivo research, as well as randomized clinical trials **(Table 1)**.

Table 1. Literature summary on the prevention and management of white spot lesions (WSLs) during fixed orthodontic treatment

Research Title and Citation	Authors and Publication Year	Goal	Methods	Outcomes
Methods to Mitigate and Address White Spot Lesions in Fixed Orthodontics [13]	Lopatiene, Borisovaite, Lapenaite (2016)	Investigate strategies to prevent WSLs using fluoride and casein-based agents	Analyzed controlled trials (2008–2016) involving fixed appliance patients, sourced from PubMed, ScienceDirect, Embase, and Cochrane Library	Fluoride and CPP-ACP agents effectively decrease WSLs; CPP-ACP may surpass fluoride rinses in preventing enamel lesions
Effectiveness of Fluoride-Based Products in Preventing Early Tooth Decay in Orthodontics [14]	Benson, Parkin, Dyer, Millett, Germain (2019)	Examine topical fluoride's ability to reduce new WSLs in orthodontic patients	Reviewed randomized trials comparing fluoride agents to placebo/no treatment, using Cochrane Library, Medline, and Embase	Toothpaste with 5000 ppm fluoride and professional 12,300 ppm fluoride foam significantly reduce new WSLs during fixed orthodontics
Fluoride Varnish Efficacy for Enamel Protection in Orthodontic Treatment [15]	Sonesson, Twetman (2023)	Assess fluoride varnish's role in preventing WSLs during orthodontic care	Evaluated randomized trials (up to 2022) with quarterly varnish applications	Consistent fluoride varnish use effectively prevents WSLs in orthodontic patients
In Vivo Assessment of Fluoride Varnish for Enamel Lesion Prevention [16]	Perrini, Lombardo, Arreghini, Medori, Siciliani (2016)	Study fluoride varnish's impact on preventing WSLs in fixed appliance patients	Conducted a split-mouth study with 24 patients, comparing varnished vs. non-varnished teeth	Regular fluoride varnish provides some WSL protection, though not significant with optimal hygiene practices
Ammonium Fluoride Varnish for Reducing White Spot Lesions [17]	Sonesson, Brechter, Abdulraheem, Lindman, Twetman (2020)	Evaluate ammonium fluoride varnish for WSL prevention	Randomized 166 patients to fluoride varnish or placebo, applied every six weeks around brackets	Ammonium fluoride varnish significantly reduces severe WSLs in orthodontic treatment
NaF vs. APF Mouthwash Efficacy in Preventing Enamel Lesions [18]	Pilli, Singaraju, Nettam, Keerthipati, Mandava, Marya (2022)	Compare weekly NaF vs. daily APF mouthwash for WSL prevention	Randomized 90 participants into two groups for a six-month study	Daily APF mouthwash is more effective than weekly NaF in preventing WSLs
Evidence-Based Approaches to Prevent and Treat Orthodontic Enamel Lesions [19]	Yazarloo, Arab, Mirhashemi, Gholamrezayi (2023)	Review strategies for WSL prevention and management	Analyzed randomized trials (2015–2020)	Fluoride toothpaste is essential; 5% fluoride varnish is advised for patients with inadequate hygiene
Self-Applied Fluoride Products for Enamel Lesion Prevention and Repair [20]	Sardana, Manchanda, Ekambaram, Yang, McGrath, Yiu (2019)	Assess self-applied fluorides for WSL prevention and remineralization	Reviewed randomized trials from Cochrane Library, Embase, Medline, and Scopus	Self-applied fluorides are moderately effective in preventing WSLs, with limited support for remineralization
CPP-ACP and CPP-ACPF for Enamel Lesion Prevention and Repair [21]	Imani, Safaei, Afnaniesfandabad, Moradpoor, Sadeghi, Golshah, Sharifi, Mozaffari (2019)	Examine CPP-ACP and CPP-ACPF for WSL prevention and remineralization	Reviewed trials from Web of Science, Scopus, PubMed, and Cochrane Library	CPP-ACP and CPP-ACPF reduce WSL incidence and enhance enamel remineralization
Amine Fluoride Mouthwash for Enamel Protection in Orthodontics [22]	Ravi Kiran, Sabrish, Mathew, Shivamurthy, Sagarkar (2023)	Assess amine fluoride mouthwash for WSL prevention	Randomized 50 patients, evaluating WSLs via intraoral photographs	Amine fluoride mouthwash significantly outperforms fluoride toothpaste in reducing WSLs
Professional Fluoride Treatments for	Babadi Oregani, Jafari, Masoud Sajedi, Reza Motamedian (2022)	Evaluate professional fluoride applications for WSL prevention	Reviewed RCTs from PubMed and Cochrane Library, covering	Multiple varnish applications or daily fluoride mouthwash

Enamel Protection in Orthodontics [23]			varnishes, gels, and mouthwashes	significantly reduce WSLs
MI Varnish and MI Paste Plus for Enamel Protection and Repair [24]	Rechmann, Bekmezian, Rechmann, Chaffee , Featherstone (2018)	Assess MI Paste Plus (MIPP) and MI Varnish (MIV) for WSL prevention	Randomized 40 patients into experimental (fluoride toothpaste, MIPP, MIV) and control groups, monitored for 12 months	Experimental group had elevated salivary fluoride, but WSL scores showed no significant difference
High-Fluoride Toothpaste for Enamel Protection in Orthodontics [25]	Sonesson, Twetman, Bondemark (2014)	Investigate high-fluoride toothpaste for WSL prevention	Randomized 424 adolescents to 5000 ppm or 1450 ppm fluoride toothpaste	Daily 5000 ppm fluoride toothpaste significantly reduces WSLs
In Vitro Comparison of Fluoride Agents for Enamel Protection Near Brackets [26]	Reddy, Manne, Sekhar, Gupta, Shivaram, Nandalur (2019)	Compare fluoride agents for preventing demineralization near brackets	Tested 100 premolars in vitro, divided into five groups with fluoride varnish, APF gel, and toothpaste	Fluoride varnish was most effective, followed by toothpaste, APF gel, and mouthwash
Optimal Methods for Preventing Enamel Lesions in Orthodontics [27]	Patano, Malcangi, Sardano, Mastrodonato, Garofoli, Mancini, Inchingolo, Di Venere, Inchingolo, Dipalma, Inchingolo (2023)	Identify effective WSL prevention strategies	Reviewed studies (2018–2023) on orthodontic patients	Fluoride toothpaste is critical; periodic professional fluoride gels and varnishes are advised
Fluoride-Based Dentifrices for Reducing Orthodontic Enamel Lesions [28]	Kau, Wang, Palombini, Abou-Kheir, Christou (2019)	Evaluate Clinpro 5000, Clinpro Tooth Crème, and MI Paste Plus for WSL prevention	Randomized three groups to use selected products for four months	Clinpro 5000 slightly outperforms Clinpro Tooth Crème and MI Paste Plus in reducing WSLs
Efficacy of Remineralizing Agents for Enamel Lesion Prevention [29]	Tahmasbi, Mousavi, Behroozibakhsh, Badiee (2024)	Compare NaF, CPP-ACPF, and Remin Pro for preventing enamel lesions	Tested 56 premolars with pH cycling and daily remineralizing agent application	NaF is more effective than CPP-ACPF and Remin Pro in preventing WSLs

Lopatiene *et al.* (2016): This systematic review updated evidence regarding WSL prevention with fluoride-based materials and/or casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) during and after fixed orthodontics. Twelve studies (clinical trials, cohort analyses, and case reports) were reviewed. Four found no measurable benefit of fluoride applications (toothpaste, varnish), while another four demonstrated clear improvements. CPP-ACP appeared more efficient than fluoride rinses for remineralization post-treatment. In total, nine of twelve studies supported the usefulness of fluoride and/or CPP-ACP for both prevention and management of WSLs [13].

Benson *et al.* (2019): This study tested topical fluoride against WSLs in orthodontic patients. Fluoride varnish showed the highest efficacy, lowering new WSL incidence (11.7%) versus placebo (29.7%). Reduced-concentration varnish had weaker outcomes. Fluoride gel every three months was not significantly different from control, while professional foam used bimonthly helped decrease lesions. High-fluoride toothpaste (5000 ppm), especially when combined with amine or stannous fluoride, outperformed conventional sodium fluoride. Overall, frequent application of high-concentration varnishes proved most effective, with concentration and application rate being critical [14].

Sonesson *et al.* (2023): This review of seven randomized controlled trials (12–26 months in duration) examined the role of fluoride varnish in WSL prevention during orthodontic treatment. Applications occurred every 4–12 weeks and included agents such as 5% sodium fluoride, 5% sodium fluoride with CPP-ACP, difluorosilane, and 1.5% ammonium fluoride. Regular varnish use led to a clear reduction in WSL occurrence, with many studies reporting decreased enamel demineralization. Combinations with CPP-ACP improved remineralization effects. Frequent, consistent varnish application was concluded to be highly effective [15].

Perrini *et al.* (2016): Using a split-mouth approach in 24 orthodontic patients, this in vivo study assessed Duraphat varnish (5% sodium fluoride). Application was either quarterly (Group 1) or semiannually (Group 2) on quadrants 1 and 3, with

quadrants 2 and 4 as controls. Over a 12-month period, minimal differences emerged across timepoints (3, 6, 9, 12 months). At nine months, however, treated incisors showed significantly less demineralization. Overall, differences between treated and untreated teeth were not substantial, and application frequency (twice vs. four times yearly) did not greatly alter outcomes [16].

Sonesson *et al.* (2020): This clinical study evaluated a new varnish containing 1.5% ammonium fluoride versus placebo in adolescents with fixed appliances for at least 12 months. Applications were performed every six weeks at orthodontic visits following biofilm removal. Both varnishes were similar in taste, appearance, and handling, except for the active component. Patients avoided food/drink for one hour post-application and brushed with 1450 ppm fluoride toothpaste. Final results indicated no significant difference in mild WSL incidence between groups, but fewer severe lesions were found in the test group at appliance removal [17].

The 2022 investigation by Pilli *et al.* compared the clinical performance of a neutral sodium fluoride (NaF) mouthrinse with that of an acidulated phosphate fluoride (APF) rinse for reducing white spot lesions (WSLs) following orthodontic therapy. Ninety patients were randomly divided into two cohorts: Group A used a 0.2% NaF rinse once a week, while Group B used a 0.044% APF rinse daily. Each participant rinsed for one minute after brushing. Evaluations occurred at 4 weeks (T1), 12 weeks (T2), and 24 weeks (T3). The NaF group exhibited a steady rise in ICDAS scores, suggesting progressive demineralization from T0 through T3. In contrast, the APF group's ICDAS scores increased until T2 but declined by T3. Statistically significant differences in the NaF group appeared between all timepoints except T2–T3, whereas the APF group showed significance only between T2 and T3 [18].

Yazarloo *et al.* (2023) carried out a literature review involving multiple randomized clinical trials to assess both preventive and therapeutic approaches for orthodontic-related WSLs. From database searches, 23 papers met the selection standards. These covered preventive measures such as CPP-ACP products, varnishes, pastes, rinses, adhesives, and sealants, along with treatment strategies including remineralizing agents, fluoride varnishes, and chlorhexidine rinses [19].

The 2019 study by Sardana *et al.* examined the effectiveness of self-applied fluoride products in preventing WSLs caused by fixed orthodontics. After a database search, three RCTs were deemed suitable: two investigated prevention, and one evaluated reversal of WSLs after treatment. The prevention studies recorded outcomes at debonding. One reported significantly fewer WSLs in patients using a 250 ppm fluoride rinse compared to placebo, while another showed that 5000 ppm NaF toothpaste was more effective than the 1450 ppm formulation [20].

The potential of CPP-ACP and CPP-ACPF formulations to prevent or remineralize WSLs was assessed by Imani *et al.* (2019). Thirteen papers were reviewed: four with CPP-ACP products and nine with CPP-ACPF. Comparisons were made against control groups (placebo, fluoride toothpaste, varnish, or rinse), with follow-up ranging from 3 to 36 months. Three trials confirmed CPP-ACP's superiority in remineralization, while one found no advantage. Four studies highlighted CPP-ACPF's clinical benefit, but five showed no significant difference from controls [21].

In 2023, Ravi Kiran *et al.* investigated amine fluoride mouthrinse as a preventive adjunct during orthodontic treatment. Patients were followed for 6 months from bonding and randomized into two groups. Group A (control) maintained standard oral hygiene with fluoride toothpaste alone, while Group B (test) added daily rinsing with 480 ppm amine fluoride. At baseline, WSL scores were comparable ($p = 0.068$). After 6 months, significant differences were noted ($p = 0.006$): the control group showed worsening scores, whereas the experimental group improved, confirming the effectiveness of amine fluoride mouthrinse in WSL prevention [22].

The 2022 review by Babadi Oregani *et al.* assessed fluoride interventions against placebo for preventing enamel demineralization. Seven eligible papers were included. In four of them, fluoride varnish was applied multiple times (4–20 applications) in the test groups, while controls received placebo or no treatment. Another trial compared two single-application varnishes against placebo. One paper tested fluoride mouthrinse versus placebo, and another compared 5000 ppm high-fluoride toothpaste to 1450 ppm standard fluoride paste. Across nearly all studies, enamel lesions were reduced in fluoride groups. However, the trial with a one-time varnish application found no significant difference versus placebo [23].

The 2018 randomized clinical trial by Rechmann *et al.* explored a combined protocol of fluoride toothpaste with MI Paste Plus (MIPP) and MI Varnish (MIV) for preventing and reversing WSLs. Forty subjects were randomly divided into experimental and control arms. The test group received quarterly MIV (10% CPP-ACP, 5% NaF) and used MIPP nightly (10% CPP-ACP, 0.2% NaF, 900 ppm fluoride). The control group followed standard care with 1100 ppm fluoride toothpaste

and 0.05% NaF rinse. The primary metric, enamel demineralization index (EDI), was assessed at baseline, 3, 6, and 12 months. At baseline, mean EDI was 37.7 in controls and 42.9 in the experimental group. After 12 months, scores shifted slightly to 41.3 (control) and 40.2 (experimental). Although the test group showed a downward trend, the difference was not statistically significant [24].

In 2014, Sonesson *et al.* examined whether toothpaste with elevated fluoride content could reduce white spot lesion (WSL) formation during orthodontic treatment with fixed appliances. Adolescents who had worn straight-wire braces for at least a year participated. One group used toothpaste with 5000 ppm sodium fluoride, while the comparison group used a standard 1450 ppm formula. Toothpaste and brushes were standardized and renewed every three months. At baseline, both groups were similar, but by treatment completion, the high-fluoride users had fewer WSLs (18.1%) compared with controls (26.6%). Minor lesions dominated in both arms, whereas more severe lesions were uncommon (1.2% vs. 2.3%) [25].

The 2019 laboratory study by Reddy *et al.* assessed five preventive regimens on extracted premolars bonded with brackets. The interventions were fluoride varnish, APF gel, fluoride toothpaste, and sodium fluoride mouthrinse, with a control group left untreated. Teeth underwent daily demineralization (pH 4.3, six hours) and remineralization (17 hours). After two weeks, varnish, APF gel, and toothpaste clearly reduced demineralization relative to controls. In contrast, sodium fluoride mouthrinse showed no measurable advantage. The study concluded that not all fluoride vehicles are equally protective [26].

A 2023 systematic review by Patano *et al.* synthesized clinical findings on strategies to reduce enamel demineralization during orthodontics. Sixteen human-based studies were included. Evidence indicated that acidic phosphate rinses used daily outperform weekly sodium fluoride rinses. Consistent use of ammonium fluoride varnish, fluoride toothpastes, and CPP-ACP also lowered WSL incidence. The review further noted that CO_2 laser treatment has potential to limit caries development. Comparisons between oxygen-based pastes and conventional fluoride toothpastes revealed no significant differences. Collectively, rinses with acidic phosphate, varnish, CPP-ACP, and standard fluoridated pastes remain reliable preventive measures [27].

In another 2019 trial, Kau *et al.* compared three remineralizing products: Clinpro 5000 (5000 ppm sodium fluoride), Clinpro Tooth Crème (950 ppm sodium fluoride), and MI Paste Plus (CPP-ACPF). Each group consisted of 40 orthodontic patients who used their assigned product twice daily for two minutes over four months. Enamel Decalcification Index scores were evaluated. Clinpro 5000 provided the strongest defense, Clinpro Tooth Crème was least effective, and MI Paste Plus showed intermediate results [28].

Also in 2019, Tahmasbi *et al.* evaluated NaF, MI Paste Plus, and Remin Pro (a hydroxyapatite-fluoride cream) using 56 enamel samples, divided into four groups. The control received only pH cycling; NaF was applied as a 0.05% rinse for five minutes; MI Paste Plus and Remin Pro were applied after artificial saliva. Following 14 days, microhardness tests indicated NaF maintained enamel hardness best, followed by Remin Pro, then MI Paste Plus, with controls showing the greatest loss [29].

The quality review of all 23 eligible studies indicated that two were low risk, two moderate, and the majority (nineteen) high risk of bias **(Table 2)**.

Table 2. Risk of bias of included RCTs using the Cochrane Collaboration tool

Research Team and Citation	Trial Design	Randomization Method	Allocation Secrecy	Blinding of Evaluators	Data Integrity	Selective Disclosure	Overall Bias Level
Benson *et al.* [14]	RCT	Low	High	Unclear	Low	Low	High
Perrini *et al.* [16]	RCT	Low	High	Unclear	Low	Low	High
Sonesson *et al.* [17]	RCT	Low	Low	Low	Low	Unclear	Moderate
Pilli *et al.* [18]	RCT	Low	High	Low	Unclear	Low	High
Ravi *et al.* [22]	RCT	Low	Low	Low	Low	Unclear	Moderate
Rechmann *et al.* [24]	RCT	Low	Low	Low	High	Unclear	High
Sonesson *et al.* [15]	RCT	Low	Low	Low	Low	Unclear	Moderate
Kau *et al.* [28]	RCT	Low	Low	Unclear	High	High	High

Discussion

A wide body of research has investigated strategies for preventing white spot lesions (WSLs) during orthodontic treatment with brackets. This subject holds particular importance because the primary objective of orthodontics is to enhance smile esthetics, while demineralized lesions can undermine treatment results and negatively affect patient satisfaction. WSLs frequently develop on the labial surfaces of maxillary incisors and have been reported in up to 96% of patients with fixed appliances [17].

Multiple clinical and experimental works demonstrate the protective role of fluoride varnishes in lowering the occurrence of orthodontically induced WSLs [16-19, 21, 25, 28, 29]. Benson *et al.* [14] stressed that professionally applied, "passive" fluoride-release systems, such as varnishes, do not rely on patient compliance and deliver fluoride precisely at critical sites. However, while many varnishes initially release high concentrations, the effect declines quickly, making repeated applications necessary. Their review indicated that reapplication every six weeks at routine check-ups did not always produce statistically significant reductions in WSLs. Similarly, Perrini *et al.* [16] followed patients for 12 months, showing lower demineralization in treated teeth, with significant benefits confined mainly to anterior teeth.

Sonesson *et al.* [15] observed that fluoride varnish exerted stronger benefits in more advanced lesions, underlining its role in preventing severe WSLs that otherwise might require interventions like resin infiltration or bleaching for esthetic correction. In another trial, Sonesson *et al.* [17] confirmed that systematic application of a 1.5% ammonium fluoride varnish (7700 ppm fluoride) reduced WSL incidence. Clinically meaningful improvements were noted, with marginal lesions remineralizing within three months after bracket removal. Similar positive outcomes were reported by Patano *et al.* [26] and Yazarloo *et al.* [19]. Reddy *et al.* [25] further identified that a varnish enriched with calcium, fluoride, and phosphate achieved stronger remineralization, attributed to its unique formulation method.

This specialized varnish incorporated beta-tricalcium phosphate and sodium lauryl sulfate, generating "functionalized" calcium and phosphate ions that enhance their uptake into enamel [25]. More recently, Babadi Oregani *et al.* [23] tested four varnishes with different fluoride levels and concluded that enamel treated with 22,000 ppm and 10,000 ppm fluoride developed higher acid resistance, though the difference between these two concentrations was not significant. Thus, increasing fluoride content up to a threshold enhances protection, reinforcing the established role of varnishes in WSL prevention [26].

Beyond fluoride alone, numerous investigations have assessed casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) and its fluoride-containing variant CPP-ACPF [13, 19, 21, 24, 28, 29]. Imani *et al.* [20] demonstrated that CPP-ACP can stabilize calcium and phosphate on enamel surfaces, supporting remineralization. Their findings showed that when combined with fluoride, CPP-ACP produced greater benefit, with daily use alongside fluoridated toothpaste reducing WSLs within one month. Nonetheless, inconsistencies remain. For example, Rechmann *et al.* [24] reported variable results regarding long-term efficacy, while other comparisons confirmed that fluoride alone remains more effective than CPP-ACP by itself.

Evidence suggests a synergistic effect when CPP-ACP and fluoride are combined. In particular, CPP-ACPF has consistently shown stronger remineralizing effects than CPP-ACP without fluoride. Several randomized trials revealed that CPP-ACP–based creams used daily in combination with fluoridated toothpastes were superior to placebo creams, producing significant reductions in WSLs within the first month [21]. Lopatiene *et al.* [13] similarly concluded that fluoride and CPP-ACP combinations were effective in limiting demineralization during orthodontics, with CPP-ACPF potentially outperforming fluoride rinses in post-orthodontic remineralization.

Yazarloo *et al.* [19] confirmed that MI Paste Plus (CPP-ACP with fluoride) provided only short-term improvements in WSLs, with limited sustained effects. CPP-ACP alone produced negligible results but showed greater benefit when paired with daily fluoride toothpaste. In contrast, Rechmann *et al.* [24] offered conflicting findings. Their trial, which tested quarterly MI Varnish, daily MI Paste Plus, and standard fluoride toothbrushing, found only small, non-significant differences. Enamel demineralization index (EDI) scores declined slightly in the intervention arm but rose in controls, though the variation was not statistically meaningful. Similarly, International Caries Detection and Assessment System (ICDAS) scores showed no major differences.

Tahmasbi *et al.* [29], in line with the findings of Rechmann *et al.*, reported that MI Paste Plus was able to partially limit enamel demineralization, but the difference compared to untreated controls was not statistically meaningful. Although it

slightly lowered lesion formation, its protective effect was weaker than that of fluoride [29]. In a similar context, Kau *et al.* [28] compared three products—Clinpro 5000 toothpaste, Clinpro Crème, and MI Paste Plus—during orthodontic therapy. They observed that MI Paste Plus was less effective, while Clinpro 5000 showed the strongest remineralization activity [28]. These results highlight the central role of fluoride agents in reducing white spot lesions (WSLs) during fixed orthodontic treatment. Repeated success with high-fluoride products indicates that consistent and controlled fluoride exposure strengthens enamel against mineral loss. Moreover, the possible complementary action of CPP-ACP with fluoride suggests the need for more research into the durability of combination treatments. Fluoride rinses and gels may also offer protection, though outcomes remain strongly dependent on patient adherence.

The present review also considered the remineralizing action of different toothpastes, ranging from high-fluoride products to those with alternative formulations [14, 19, 20, 25-28]. Benson *et al.* [14] stressed that fluoride toothpastes can be effective only if applied regularly, making patient compliance the deciding factor for success. Yazarloo *et al.* [19] found that brushing twice daily for two minutes with Clinpro 5000 or Clinpro Tooth Crème reduced WSLs effectively, producing results similar to MI Paste Plus. Kau *et al.* [28] also reported that Clinpro 5000 gave the lowest enamel demineralization index (EDI) among tested groups, confirming its slightly superior performance. Patano *et al.* [27] supported this conclusion and added that oxygen-releasing toothpaste performs just as well as fluoride products. Sonesson *et al.* [25] further demonstrated that high-fluoride toothpaste decreases biofilm metabolic activity, acting at the biofilm–tooth interface to limit demineralization and promote remineralization [25].

Sardana *et al.* [20] reached similar conclusions, showing that higher fluoride concentration provided greater protection against WSLs compared to low-fluoride paste. Consistently, Reddy *et al.* [26] reported significantly better results for patients using fluoride toothpaste than for controls. In addition to fluoride varnishes and CPP-ACP products, this review also examined mouthwashes and their preventive potential [18, 19, 22, 26, 29]. Pilli *et al.* [18] compared an acidulated phosphate fluoride (APF, 0.044% NaF) rinse with a 0.02% NaF rinse. After the first month of orthodontic treatment, both groups showed new enamel demineralization and early caries, confirming that complete prevention of WSLs is unrealistic. However, daily rinsing with the APF solution was more effective than weekly rinsing with neutral NaF [18].

Tahmasbi *et al.* [29] also compared sodium fluoride rinse with MI Paste Plus and Remin Pro. Their findings showed that enamel microhardness remained most stable in the NaF group, indicating it was the most protective option [29]. In contrast, Reddy *et al.* [26] reported only slightly better outcomes with NaF mouthwash compared to controls, without statistical significance. Ravi Kiran *et al.* [22] tested a low-dose ammonium fluoride rinse and found a significant reduction in WSL scores compared with patients using only fluoride toothpaste, with lower lesion prevalence in the rinse group. Sardana *et al.* [20] likewise demonstrated that rinsing with 250 ppm fluoride (150 ppm NaF + 100 ppm ammonium fluoride) significantly lowered WSLs compared with placebo, underscoring the preventive role of self-applied fluorides.

The limitations of this review include restricted database access—Science Direct and Web of Science were unavailable due to subscription issues, and although Medline was searched, access through the proxy was blocked. Another drawback was the high variability among studies, preventing quantitative synthesis. Future work should classify WSLs by stage to track progression and explore whether outcomes improve more with fluoride, CPP-ACP-based products, or newer approaches. Novel biomaterials such as nanohydroxyapatite should also be investigated as potential remineralizing agents. Randomized controlled trials comparing fluoride concentrations and delivery systems could provide clearer clinical recommendations. Finally, artificial intelligence may contribute by tracking oral hygiene compliance and detecting early lesions, thereby strengthening preventive orthodontic care.

For upcoming randomized controlled trials, several aspects need to be carefully addressed: ensuring adequate sample sizes, proper allocation concealment by independent parties, blinded outcome assessment at both patient and tooth levels, and the use of a standardized and validated outcome set. In addition, greater focus should be placed on incorporating WSL-prevention strategies into everyday orthodontic protocols. More evidence is also required to define reproducible guidelines for the clinical use of lasers. Numerous investigations have tested toothpastes and related products with antibacterial properties, and many have yielded promising findings that justify continued research. Orthodontists should remember that correcting malocclusions must be aligned with preserving the patient's oral health, and it is expected that preventive programs for caries and demineralization will receive growing attention and support.

Conclusions

White spot lesions represent one of the most frequent and troublesome side effects of fixed appliance therapy, as they can undermine both the aesthetic and functional outcomes of treatment. The literature reviewed in this paper emphasizes the importance of minimizing these lesions during conventional orthodontics with brackets. In this regard, the joint role of orthodontists and dental hygienists is crucial, particularly in educating and motivating young patients, who are often undergoing treatment during adolescence, a sensitive period of development. Maintaining excellent oral hygiene, supported by high-fluoride dentifrices and rinses, should be part of every patient's routine. Nevertheless, these measures alone may not always be sufficient to ensure optimal protection. Orthodontic treatment is designed to improve not only oral health and function but also smile aesthetics, and WSLs can compromise the overall benefit of long-term therapy. Therefore, complementary measures such as fluoride varnishes and casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) formulations—both of which have demonstrated preventive and remineralizing effects—should be considered to reduce lesion occurrence. Incorporating evidence-based strategies into daily care, especially passive fluoride interventions for patients with low compliance, is highly recommended. Tailored hygiene instructions combined with remineralizing products may provide a more comprehensive preventive approach.

Future work should aim at refining intervention protocols, assessing the durability of preventive outcomes over time, and determining effective ways to enhance patient compliance. While this review offers valuable insight into prevention, its limitations must be acknowledged. Considerable heterogeneity in methodologies and intervention protocols across studies complicates the ability to draw firm conclusions. Furthermore, most available trials are short-term, making it uncertain whether remineralization effects persist once appliances are removed. To address these gaps, future research should standardize study design and conduct long-term randomized trials to confirm the effectiveness of preventive measures. However, the current body of literature still does not provide unanimous evidence regarding the efficacy of different products, as results remain inconsistent across studies.

Ultimately, prevention of WSLs begins with selecting and motivating patients to maintain high standards of oral hygiene. The foundation of this effort is daily brushing with fluoride-containing toothpaste, which helps remove food debris and plaque accumulation around orthodontic hardware. Depending on the clinical case, additional fluoride delivery systems—including rinses for home use and gels, varnishes, or sealants applied professionally—can be integrated to enhance protection.

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