Status and progress of treatment methods for root caries in the last decade: a literature review

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Abstract

Abstract: The aim of this literature review is to explore the treatment methods for root caries in laboratory and clinical research in the last decade. A systematic search of publications in PubMed and Web of Science databases was performed. The time-span was limited to the last 10 years and English language. Further retrieval was conducted using the search terms of specific therapies or treatments. Titles and abstracts of identified publications were screened. Reviews; case reports; conference abstracts; letters to editor; dissertation and theses; non-English articles; epidemiological studies, diagnostic methods or decision-making process for root caries treatment without assessment of its efficacy; deep carious lesions with inflamed pulp and require pulp capping or endodontic treatment and research on root cementum were excluded. The remaining papers were retrieved with full-texts. Cross-referencing was performed to identify other relevant articles in addition to manual screening of the bibliographies of the remaining papers. Eighty-two articles were included in this systematic review and full texts were retrieved. Types of studies included laboratory studies and clinical trials. Therapeutic approaches for root caries without risk of pulp exposure can be categorised into non-invasive and restorative treatment. Non-invasive treatments which targeted different causative factors of root caries have been developed in the last decade. Accordingly, several artificial caries model systems have been proposed for the study of root caries in the laboratory. Carious tissue excavation techniques and restorative materials and procedures have been modified to improve the prognosis of invasive treatment. It is of importance to determine the most appropriate therapy for root caries and further clinical trials are needed to draw firm conclusions concerning the efficacy and consistency of the various treatment methods proposed.

Key words: root caries, dentine, treatment method, systematic review

Introduction

Elderly people make up an increasing share of the world's total population due to the dramatic increase in average life expectancy.[1] A larger proportion of elderly individuals now retain their teeth longer due to advances in oral health care and treatment.[2] Accordingly, the oral health problems of the elderly are shifting from complete tooth loss towards untreated carious lesions.[3] In addition, gingival recession occurs frequently in elderly people and the exposed root surfaces increase the risk of root carious lesions (RCL; a carious lesion situated on the root surface) development and progression. Untreated RCL are now peaking later in life and root caries experience can be expected to continually increase in future years.[4]

Multiple risk factors contribute to the prevalence and progression of RCL in the elderly, such as impaired oral hygiene resulting from poor oral care behaviours, drug-induced salivary flow reduction, complex health status due to concomitant systemic diseases and frequent snacking at home.[5] The success of treatment of RCL in this caries-susceptible group can be challenging, especially for those with limited mobility, inadequate financial resource or lack of dental health insurance.[6, 7] Also, traditional restoration placement may be hampered by difficulties in moisture control on root surfaces, as the RCL can extend sub-gingivally. With dentine as the only adherent substrate, the reliability of adhesion is also less predictable.[8] Therefore, there is a continuing need for alternative techniques for RCL management.

Several reviews have critically evaluated the treatment methods for RCL from a specific aspect, such non-invasive approaches, therapeutic agents used in the treatment, as well as from a periodontal perspective.[9-12] The validity of the treatment approaches proposed decades ago (e.g. 1100-1450 ppm fluoride dentifrice) have been well established. Advances in knowledge regarding cariology and aetiological factors in recent years has given rise to novel approaches, with emphasis on the protection of the organic matrix in dentine and from the perspective of biomimetic remineralisation, especially in laboratory studies.[13, 14] Also, the concept of minimal intervention dentistry (MID) has been emphasized if restorative treatment is necessary.[15] Unlike previous research which mainly addressed restorative material options, recent studies have concentrated more on the improvement and modification of restorative materials as well as procedures in order to arrest the disease process and improve restoration longevity. As root caries is becoming an increasingly important oral health concern, research in this area has accelerated during the last decade. It is of significance to update previous knowledge and provide a general overview of developments in RCL management both from laboratory studies and clinical trials.

This literature review aims to categorise and critically evaluate the treatment methods for RCL over the past decade (from 2007 to the present) and provide recommendations for future research and clinical practice. Both laboratory studies and clinical trials are included and methods to model RCL in vitro are summarised.

Materials and Methods

A database search was performed in PubMed and Web of Science for articles published in the last decade. The last search was made on 28, February, 2017.

The search terms used for this review were:

Initial Retrieval:

PubMed

((("dental caries"[MeSH Terms] OR ("dental"[All Fields] AND "caries"[All Fields]) OR "dental caries"[All Fields] OR "caries"[All Fields]) OR carious [All Fields]) AND ("root"[All Fields])) AND ("therapy"[Subheading] OR "therapy"[All Fields] OR "treatment"[All Fields] OR "therapeutics"[MeSH Terms] OR "therapeutics"[All Fields]). Publication dates: in 10 years. Languages: English.

Web of Science

TOPIC = (caries OR carious) AND TOPIC = (root) AND TOPIC = (therapy OR treatment OR therapeutics)) AND LANGUAGE: (English)

Timespan = 2007-2017

Further retrieval:

PubMed

(("root"[All Fields]) AND ("dentin*"[MeSH Terms] OR "dentin*"[All Fields]) AND ("dental caries"[MeSH Terms] OR ("dental"[All Fields] AND "caries"[All Fields]) OR "dental caries"[All Fields] OR "caries"[All Fields]) AND ("restoration" [All Fields] OR "amalgam" [All Fields] OR "resin composite"[All Fields] OR "glass-ionomer cement" [All Fields] OR "glass-ionomer cements" [All Fields] OR "remineralization" [All Fields] OR ("anti-bacterial agents"[Pharmacological Action] OR "anti-bacterial agents"[MeSH Terms] OR ("anti-bacterial"[All Fields] AND "agents"[All Fields]) OR "anti-bacterial agents"[All Fields] OR "antibacterial"[All Fields]) OR ("laser"[MeSH Terms] OR "laser"[All Fields] OR "lasers"[All Fields]) OR ("Atraumatic Restorative Treatment" [All Fields] OR "ART restoration" [All Fields] OR "ART technique" OR "ART") OR ("collagenases"[MeSH Terms] OR "collagenases"[All Fields] OR "collagenase"[All Fields]) OR ("fluorides"[MeSH Terms] OR "fluorides"[All Fields] OR "fluoride"[All Fields]). Publication dates: in 10 years. Languages: English.

Web of Science

TOPIC = ((caries OR carious OR dental caries) AND TOPIC = (root) AND TOPIC = (dentin) AND TOPIC = (fluoride OR laser OR restoration OR Atraumatic Restorative Treatment OR ART OR antibacterial OR resin composite OR glass-ionomer)) AND LANGUAGE: (English)

Timespan = 2007-2017

Cross-referencing was performed to identify further articles.

Study selection:

The search was limited to English-language journals and papers published between 2007 and 2017. Studies selected met the following inclusion criteria:

Types of studies:

Studies included in the present review were laboratory studies or clinical trials (Level I or II). The following types of studies were excluded: reviews; case reports; conference abstracts; letters to editor; dissertation and theses.

Intervention:

Either invasive or non-invasive treatments on RCL with no risk of pulp exposure were included. Deep RCL affecting dental pulp which involved endodontic treatment such as root canal therapy and pulp capping and studies concentrating on diagnostic methods or decision-making process for RCL treatment without assessment of efficacy were excluded.

Control:

Negative (placebo treatment), positive (other intervention or frequently used standard therapy, e.g. conventional fluoride toothpaste)

Data extraction:

Study type (clinical trial, laboratory study on human/bovine dentine or in situ trial), pharmaceutical agents or methods used for interventions, type of intervention (invasive or non-invasive approaches), type of control group, and assessment of intervention by measurement of outcomes which clearly indicated the effects of certain treatment (e.g. decayed-missing-filled root surface, root caries incidence, hardness, lesion depths).

Results

In total, 1102 articles (808 in PubMed, 482 in Web of Science, with 188 duplicates) were identified by screening electronic databases. For further refinement, publications were limited to those from the scientific, peer-reviewed and English literature. Titles and abstracts of articles were read and the following papers were excluded: Reviews; case reports; conference abstracts; letters to editor; dissertation and theses; non-English articles; epidemiological studies, diagnostic methods or decision-making process for root caries treatment without assessment of its efficacy; deep carious lesions with inflamed pulp and require pulp capping or endodontic treatment and research on root cementum. After screening, 60 papers remained for inclusion. Further retrieval was conducted using specific terms of treatment strategies. An additional 22 publications were identified (10 in Web of Science, 12 in PubMed). No articles were identified by cross-referencing. (The searching process was also undertaken to retrieve articles published between 1900-2006. The majority of the treatment methods in these papers have been reconfirmed or updated in the research in recent years, thus with less novel insights. Therefore, only literature published during the last decade (2007-2017) were included.)

A total of 82 of articles, including 46 laboratory studies, nine in situ experiments and 27 clinical trials were screened for full-text analysis. In the clinical trials, five studies were considered as Level I b randomised controlled trials (RCTs),[16-20] with adequate and appropriate description of random allocation sequence generation and allocation concealment as well as a reasonable sample size, the other studies were graded as level II evidence, with unclear or inadequate explanation of the randomisation process or with a follow-up of less than 80%.[21] Laboratory studies were performed on either extracted bovine or human teeth. The nine in situ studies employed special palatal or buccal appliances to place the tooth specimens in patients' mouths for exposure to the oral environment.[22-29] (Fig. 1)

Figure 1 Flowchart of search strategy.

Root caries manifests as a continuum of disease with increasing severity. The disease state could progress from an initial asymptomatic status to RCL leading to tooth destruction. When diagnosing RCL, it is of importance to distinguish between active and inactive/arrested lesions, thus determining the most favourable management strategies.

Treatment methods for RCL can be categorised into non-invasive approaches and restorative (surgical) treatment. The non-invasive approaches are generally based on several mechanisms and strategies listed in **Table 1**.

1 Non-invasive management of RCL

1.1 Fluoride formulations

Thirty-one articles, which included 11 laboratory studies, six in situ studies and 14 clinical trials, investigated the application of fluoride-containing products such as dentifrices, varnishes, mouthwashes and milk, or an adjunctive use of fluoride with other 'active' components like triclosan,[30] arginine,[19, 31] casein phosphopeptide-amorphous calcium phosphate (CPP-ACP),[32] calcium sodium phosphosilicate[33] or supersaturated mineralising ions.[34] One laboratory experiment explored the role of hydroxyapatite nanoparticles on remineralisation of artificial RCL.[35]

Undisputed evidence has revealed that fluoride is effective in the prevention and treatment of carious lesions.[36] The anti-caries effect of fluoride is related to its ability to alter ionic saturation characteristics with respect to tooth mineral and aid remineralisation and prevent demineralisation. Also, at high concentration it may interfere with bacterial metabolism and acid production. Fluoridated products are the most widely described and most extensively used agents for carious lesion management. As dentine is more caries-susceptible than enamel due to the considerable difference in mineral composition, more researchers have begun to investigate the effects of fluoride for dentine and RCL.[28, 37]

Toothpastes containing fluoride have been considered as the most rational topical fluoride delivery vehicle and are the major source of fluoride in some communities where water fluoridation is not available.[38] The effect of frequently-used standard fluoride (1000-1450 ppm) toothpaste in reducing coronal caries experience has been well established, but its effect on dentine and RCL has not been extensively explored.[39] A two-year follow-up study amongst community dwelling elders using fluoride toothpaste showed a lower incidence of RCL and greater reversal of caries activity of non-cavitated carious lesions.[40] Evidence from several publications indicated a dose-response outcome of fluoride treatment. Specifically, a laboratory study showed that 5000 ppm fluoride dentifrice was more effective for controlling RCL formation and progression than a fluoride concentration of 1300 or 1500 ppm ($P<0.05$)[41]. In addition, toothpastes with higher fluoride concentration (5000 ppm and 2800 ppm) improved the acid resistance of bovine root dentine more effectively than 1450 ppm fluoride toothpaste.[33] The dose-dependent property was further confirmed in a clinical trial where 5000 ppm fluoride toothpaste controlled RCL progression more efficiently among elders than the regular toothpastes of 1000 ppm to 1450 ppm fluoride.[42] However, a large variability of the improvements was observed among participants with 5000 ppm fluoride treatment in a multi-centre clinical trial according to the standard deviation of surface hardness data.[20] Further to this, a pilot in situ study indicated that 1100 ppm fluoride toothpaste was enough to reduce root dentine demineralisation in a high cariogenic environment, however the sample size was relatively small.[23] Follow-up clinical trials are necessary to confirm if use of higher fluoride concentration should be considered as the best practice for RCL management.

The effectiveness of fluoride dentifrices is not only determined by fluoride concentration but also the frequency of use. Fluoride should be constantly available in the oral fluids to maximise its effect. An in situ study demonstrated a positive correlation between the frequency of use and the reduction of root dentine demineralisation, although no significant association was found between the frequency and the remineralisation of existing carious tissue.[26]

In order to improve the clinical effectiveness of fluoride dentifrices, especially in severe acidogenic conditions, new approaches have focused on incorporation of other active ingredients, especially calcium and phosphate to enhance existing salivary sources. Fluoride can reverse and arrest early dentine lesions by driving calcium and phosphate back into the lesion as low solubility fluorapatite ($Ca_5(PO_4)_3F$). Together with soluble calcium and phosphate ions, fluoride further enhances the remineralisation process. Calcium sodium phosphosilicate bioactive glass (NovaMin) has been added to a fluoride dentifrice (ReNew paste, Sultan Healthcare, PA, USA). When contact with water occurs, NovaMin dissolves and releases its inorganic calcium, sodium, and phosphate ions that putatively initiate remineralisation of the lesions, however surface precipitation due to the poor stability of the ions is likely to be the major net activity.[43] Clinically, remineralising toothpaste, supplied with fluoride, calcium and phosphate ions, was especially beneficial for patients after head and neck radiation or those with hyposalivation who have limited availability of calcium and phosphate ions in the reduced quantity of saliva. The toothpaste significantly lowered the incidence of RCL than the solely fluoride containing dentifrice.[34, 44]

As fluoride does not directly target on the reduction of dental plaque which is the major aetiological factor in conjunction with diet rich in fermentable carbohydrates, components with caries-preventive benefits have been added to fluoride dentifrices to complement the effects. Being a non-fermentable sugar substitute, xylitol inhibits glycolysis and enzymes involved in the metabolism and growth of Streptococcus mutans or induces less virulent strains of cariogenic bacteria.[45] Specifically, a highly controlled randomised clinical trial demonstrated that xylitol lozenges had a significantly pronounced caries-preventative effect on root surfaces compared to the sucralose sweetened placebo lozenge, though not on coronal surfaces, probably because of the differences in composition and virulence between root and coronal biofilms related to anatomic factors.[46] However, no significant reduction in lesion depth formation was observed with the addition of xylitol into the fluoride dentifrice. This might be attributed to a lack of biofilm in the experimental physicochemical model used in this laboratory study where xylitol hardly showed any effect on bacterial metabolism.[47] In addition, factors that increase biofilm pH can modify caries susceptibility. Arginine, as a semi-essential amino acid, can be metabolised to ammonia that helps to neutralise plaque acids, thus reducing caries initiation. Fluoride dentifrices containing 1.5% arginine were shown to re-harden more RCL than a matched fluoride dentifrice, indicating the supplementary benefit to the established effects of fluoride dentifrice.[19, 31]

Antibacterial agents, such as triclosan, are added into fluoride toothpaste. Triclosan is a chlorinated aromatic compound that has functional groups of phenols with antibacterial properties. A three-year clinical trial among adults revealed a significantly lower Katz Root Caries Index (expressed as a percentage of number of root surfaces with RCL/number of surfaces with gingival recession[48]) value in the triclosan group (Colgate Total, Colgate-Palmolive Company, NY, USA) than an identical fluoride toothpaste without triclosan.[30]

Methods of topical fluoride delivery have also been developed as mouth-rinses, gels, milk-additives and varnishes. Different fluoride formulations are chosen according to the purpose of fluoride use and target group of people. Bovine milk fluoridation is a convenient and cost-effective way of targeted fluoride supplementation, which was firstly proposed in school-based milk fluoridation programs for children at a concentration of 5 ppm F^-. Recently milk fluoridation has been considered for managing RCL. Daily intake of milk supplemented with 5 ppm fluoride has been reported to have a reversing effect on RCL in older adults in a clinical trial. However, limitations existed regarding the high drop-out rate, and methods of outcome measurement.[49] Also, the subjects were supplied with fluoride toothpaste which would most likely exert an additional effect. In a laboratory study using a S. mutans biofilm model with pH-cycling, 5 ppm fluoridated-bovine milk reduced decrease in surface hardness of dentine compared to milk only, although with no statistically significant difference.[50] Whether a 5 ppm fluoride concentration in milk is enough to achieve an optimal anti-caries effect on root dentine remains controversial. Moreover, other components in milk, such as protein, fat and other minerals may influence its protective effect, possibly because they serve as a physical barrier against the acids or buffer related caries initiation and progression.[50, 51] A dose-dependent effect of fluoridated milk was reported.[52]

Patients with hyposalivation or who have undergone radiotherapy in the head and neck region are at high risk for root caries because of the reduction in salivary flow rate. Topical fluoride application might be insufficient to control RCL in this group of people due to the decreased amount of intrinsic Ca^{2+} and PO_4^{3-} to drive remineralisation. Use of varnish is able to deliver high concentrations of fluoride, which has been recommended among moderate- to high-risk patients. Topical 5% sodium fluoride (NaF) varnish (Colgate-Palmolive Company, NY, USA) has been tested in a group of participants with Sjögren's syndrome in a 24-month clinical trial. However, no clear evidence of its preventive effects in this group of patients was determined, probably attributable to an insufficient sample size and limited length of the study.[18]

An alternative approach to address the effects of reduced salivary flow amongst these groups of people uses calcium and phosphate ion supplementation along with fluoride; designed to mimic the supersaturation of those ions in normal saliva. Regular use of a supersaturated Ca^{2+}/PO_4^{3-} rinse in conjunction with commercially available 1.1 % NaF showed its protective effect against caries progression in hyposalivating patients in a long-term study (up to 5 years).[44] In addition, Ca^{2+} and PO_4^{3-} at high concentrations can be stablised in a metastable solution using casein phosphopeptides (CPP) as the stabilizing agent, creating nanocomplexes (CPP-ACP).[53] The addition of 10% CPP-ACP paste to topical fluoride applications was observed to significantly reduce incidence of soft RCL in cancer patients subjected to head and neck radiotherapy.[32]

The combined application of several fluoridated-products contributed to some additive effects for dentine caries prevention, which ensure a high fluoride concentration at oral surfaces or in saliva. Daily regular use of 1100 ppm-fluoride dentifrice combined with acidulated phosphate fluoride (APF) gel (12 300 ppm F) application enhanced the availability of fluoride in biofilm fluid and significantly reduced the surface hardness loss and integrated mineral loss compared with the 1100 ppm dentifrice alone when using in situ models.[28] However, the combined use of APF gel (12 300 ppm F) with 1100 ppm fluoride dentifrice or 22 600 ppm fluoride varnish with 1450 ppm fluoride dentifrice was not as comparatively effective as a higher 5000 ppm fluoride dentifrice in inhibiting and repairing dentine caries lesions.[25, 54] Also, the sole use of fluoride dentifrice three times-a-day exhibited a higher caries-inhibiting effect than 'twice-a-day' even with a combined use of a fluoride mouthwash.[55] It was suggested that the treatment effect of fluoride could be not only ascribed to the fluoride component but also to the mode of application.[12]

Sodium fluoride and sodium monofluorophosphate (NaMFP) are the most commonly used fluoride agents for toothpastes.[39, 56] Their mechanism of action is attributed to the precipitation of a low acid-resistant calcium fluoride (CaF_2)-like layer on the tooth surface as a 'mechanical barrier' or the bioavailability as plaque F reservoirs in the types of either mineral CaF_2 or biological/bacterial Ca-F (the reaction between fluoride and the intercellular or intraculluar Ca 'bridge' forming Ca-F bonds at fixed bacterial sites).[57] However, it has been suggested that the fixation of fluoride would be enhanced if it is bound to a polyvalent metal such as titanium or tin, creating titanium fluoride (TiF_4) or stannous fluoride (SnF_2).[58, 59]

Titanium ions from TiF_4 may reduce demineralisation by binding phosphate from apatite and forming a glaze-like layer on the tooth surface. The titanium-rich deposits were comparatively acid-resistant with a greater protective effect compared to NaF and SnF_2.[60] TiF_4 application in a low-concentration solution and high-concentration varnish were effective against root dentine erosion.[61] Moreover, acidic zinc fluoride (ZnF_2/HCl) was investigated in laboratory research and exhibited inhibitory efficacy on dentine demineralisation and collagen degradation.[62] Although the polyvalent metal ions have demonstrated their unique advantages in conjunction with fluoride, the sustainability of their effects and their cytotoxic effects need further investigation. Organic fluorides such as amine fluoride (AmF) compounds have also shown superior anti-cariogenic properties. The amine (organic) component has an antiplaque effect and a tensioactive property which allows accumulation of fluoride close to the tooth surface.[63] The results of a one-year clinical trial indicated the potential of toothpaste and mouth-rinse containing AmF in remineralising active soft and leathery primary RCL in an adult high caries risk population.[64]

1.2 Commercialised available fluoridated sealants used for root caries prevention

When root surfaces are exposed as a result of gingival recession, some areas may be prone to rapid RCL initiation. In this regard, root surface sealants such as desensitisers and adhesives, which contained effective anti-caries components such as fluoride, chlorhexidine (CHX) and calcium-fluoroaluminosilicate, can be used on these susceptible areas to provide direct physical protection with a simple application, thus serving as an adjunctive option for the prevention of RCL. Their effects were assessed in seven papers.[27, 65-70]

Coating root surfaces with adhesive materials has been regarded as a promising procedure to prevent demineralisation.[71] A fluoride releasing material was incorporated into adhesives, i.e. Giomer products,[72] using a novel technique by pre-reacting acid-reactive glass containing fluoride with polyacrylic acid in the presence of water, which is presented as a stable glass-ionomer phase in fillers. Root dentine specimens coated with this adhesive showed decreased susceptibility for biofilm formation and increased acid resistance, thus protecting the root surface from carious lesion development.[66, 70]

Fluoride-containing resin-based desensitizing agents were first introduced to treat dentine hypersensitivity by penetration and precipitation of calcium fluoride within the dentinal tubules resulting in tubular occlusion.[73] They are currently used as an adjunctive option for the prevention of RCL, as they are able to enhance the chemical resistance of dentine to mineral dissolution against an acidic challenge and the polymerized resin layer is able to act as a physical barrier. Also, fluoride ions have been incorporated into a delivery carrier or vehicle, such as a polymer or a silicate glass, which exerted an additional benefit.[67-69]

1.3 Cross-linkers

Organic components of type I collagen fibrils are embedded with mineral crystallites in root dentine, and play an important role in the demineralisation and remineralisation process. After depletion of the mineral phase of dentine, the exposed collagen fibres are fragile and easily attacked by enzymes. The irreversible destruction makes remineralisation difficult to achieve. Herein, attempts have been made to preserve and stabilise the dentine collagen matrix.

Several naturally-derived cross-linkers, such as hesperidin (HPN),[74, 75] grape seed extract (GSE),[76, 77] Galla chinensis extract (GCE),[78] green tea extract (GTE),[79] naringin and quercetin[80] have been applied on root dentine surfaces in laboratory studies. The role of cross-linking agents to decrease proteolysis in root caries have been extensively studied in 11 papers. However, the cross-linking agents have only been investigated in laboratory-based studies with no clinical trials so far.

Most of the natural cross-linkers are bioflavonoid polyphenol-rich agents with the chemical structure based on a phenyl ring bearing a hydroxyl group. The interaction of natural cross-linkers with the collagen fibres via covalent, ionic, hydrogen bonding or hydrophobic interactions stabilises the collagen matrix. Significantly lower values of lesion depth and mineral loss during laboratory pH cycling indicated the cross-linkers' potential in inhibiting demineralisation and promoting remineralisation in natural RCL. Their effects could be enhanced when combined with other remineralising agents, such as tri-calcium phosphate (TCP), casein phosphopeptide-amorphous calcium fluoride phosphate (CPP-ACFP) and fluoride in laboratory studies.[81, 82] Synthetic cross-linking agents have also been used, among which the most widely applied is 5% glutaraldehyde. It has been incorporated in commercial adhesive systems, such as iBond (Heraeus Kulzer, Germany) and Gluma comfort Bond + desensitiser (Heraeus Kulzer, Germany). Reduced mean lesion depth was observed during pH cycling after treatment with the adhesives, indicating their potential to aid in RCL prevention.[83] However, no cross-linkers have been tested in clinical trials as yet and their mechanism in remineralisation requires further investigation, not to mention the potential to stain the root dentine.

1.4 Collagenase inhibitor

A group of collagenolytic proteinases in dentine, for instance, matrix metalloproteinases (MMPs) and cysteine cathepsins, participates in the caries process of dentine by degrading the denuded organic matrix after demineralisation. Collagenase inhibitors are considered to be effective in decreasing RCL progression by suppressing enzyme activity. Application of MMP inhibitors in the prevention of dentine destruction has been identified in two laboratory studies, which include CHX, green tea extract and a new active collagenase inhibitor - pirocton olamine (PO).[79, 84]

Chlorhexidine has been reported to inhibit the activity of several host-derived proteases, such as MMP 2, 8, and 9, thereby protecting the exposed collagen matrix from denaturation.[85] It is now often used as a positive control to test the efficacy of other MMP inhibitors. Several aforementioned crosslinking agents, such as proanthocyanidin, green tea extract and 1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) exhibited inhibitory effects against endogenous collagenases.[79, 86, 87] Efforts are still made in seeking new active collagenase inhibitors, such as pirocton olamine (PO) which has a large hydrophobic benzoic ring and alkyl chain that contributes to the interaction with enzymes.[84] However, most studies were undertaken on coronal dentine. Future studies should concentrate on providing direct evidence of changes of enzyme activity in root dentine after exposure to these collagenase inhibitors.

1.5 Antibacterial agents

As dental caries is a biofilm-mediated disease of dental hard tissues, the application of antibacterial agents has a direct effect on dentine caries. Antibacterial therapeutics in RCL have been well-documented in 10 articles. The agents for the suppression of cariogenic microorganisms ranged from silver diammine fluoride (SDF; $Ag(NH_3)_2F$) to CHX.[16, 17, 22, 88-93] Application of ozone was mentioned in one study, which was stated to have the clinical potential to reverse RCL or inactivate most of the organisms on dentine.[94]

Chlorhexidine acts as a broad-spectrum antimicrobial agent suppressing the growth of selected cariogenic bacteria (Streptococci, Lactobacilli, Actinomycetes) in the oral biofilm on root surfaces.[89, 90] However, the available evidence supporting CHX as a caries-protective agent is inconclusive. An in situ study using a commercially available 0.2% CHX mouthrinse (Corsodyl; GlaxoSmithKline, Zeist, The Netherlands) failed to show greater protection of dentine against demineralisation compared to saline. However, CHX mouthwash was shown to be more effective in inhibiting putative root-caries bacteria than Listerine (an antiseptic mouth rinse containing a combination of essential oils, e.g. menthol, thymol, methyl salicylate and eucalyptol) or Listerine with Fluoride (IDS Manufacturing, Thailand) in a laboratory study.[91] Nevertheless, CHX mouthwash was not suggested as a first-choice caries-protective agent as it may disturb the oral micro-ecological balance and the real oral environment is different from the laboratory established biofilm.[90] Cervitec (Ivoclar Vivadent, Liechtenstein), a CHX-thymol varnish (1% CHX), helped to arrest the progression of established RCL and reduce the incidence of new lesions, being applied as a simple, quick and non-invasive method among institutionalised elderly.[22, 92]

Silver diammine fluoride has an intense antibacterial effect on multi-species cariogenic biofilms (such as S. mutans and Actinomyces naeslundii) on tooth surfaces due to the antimicrobial effect of silver.[95] Thirty-eight percent SDF solution was not only effective in preventing new coronal caries in children, but has also been considered as a novel root caries preventative strategy among community-dwelling elders. The intervention of an annual SDF application was shown to be preferable to solely oral hygiene education (OHE) or oral hygiene instruction (OHI) in preventing new RCL over a 24-month period.[16, 88] However, no significant difference was found in the effectiveness in preventing RCL between SDF and other therapeutic interventions such as 1% CHX varnish or 5% NaF varnish. Thus, these three agents have similar advantages when used in clinical and community programs.[88] As silver ions in the SDF solution can cause black staining, potassium iodide (KI) can be applied immediately after the application of the SDF as the iodide ions will react with the excess silver ions and form a precipitate of silver iodide, thus reducing the staining. Results from a clinical trial showed that application of KI did not influence the effectiveness of SDF in arresting active root caries.[17]

Ozone (O_3) can act as a disinfectant and degrade to harmless, non-toxic and environmentally safe oxygen molecules. The antimicrobial effect of aqueous ozone or ozone gas was first assessed in a laboratory study.[96] There has been only one randomised clinical trial testing the efficacy of ozone for the management of 'leathery' RCL in the last decade. In this 6-month follow-up study, a portable apparatus was used to deliver ozone at a concentration of 2100 ppm ± 10% either for 10 or 20 seconds. The treatment regime using ozone dramatically reduced most of the micro-organisms in leathery root caries and led to rehardening of some of the non-cavitated leathery RCL. This improvement might be maintained when ozone was reapplied regularly.[94] However, methodological concerns exist within studies in ozone therapy in the aspects of blinding, standardized methods of outcome measurement, sample size and length of studies. Extensive clinical evidence for ozone application is needed before it can be supported.

1.6 Surface modification with lasers

Dentine surface modification, which is generally defined as morphological and chemical changes of dentine, might be beneficial for root caries resistance.[97] It is frequently conducted by the application of lasers. Laser technology is increasingly finding a useful place in dentistry, especially in management of carious lesions. The mineral of dentine, i.e. impure carbonated hydroxyapatite, has intense absorption bands in the mid-infrared (MIR) region due to phosphate, carbonate and hydroxyl groups in the crystal structure.[97-99] Every laser has a gain medium to produce the laser light which can be a gas, a fluid or a solid state and the frequently-used ones for altering dental hard tissues include CO_2 laser, free electron laser (FEL) and erbium, chromium: yttrium-scandium-gallium-garnet (Er, Cr: YSGG) laser. Studies retrieved have focused on their effects as well as exploring the optimum energy density and wavelength, with three using a CO_2 laser, one using a mid-infrared free electron laser[97] and two using an erbium; chromium: yttrium-scandium-gallium-garnet (Er, Cr: YSGG) laser.[100, 101]

1.6.1 CO_2 laser

CO_2 laser, with a wavelength of 10.6 μm is highly absorbed by carbonated hydroxyapatite, significantly reducing root surface demineralisation.[99] The most frequently mentioned hypothesis for its mechanism is based on the thermal effects of irradiation leading to ultrastructural and crystallographic changes. Moreover, only a small variation was detected in the pulp temperature when irradiated with a CO_2 laser at an energy density of 6-11 J/cm^2 for 10-20 s, much less than the irreversible damage temperature change of 5.5 ℃, indicating the safety of irradiation.[24, 102, 99] Combination of fluoride sources and CO_2 laser irradiation achieved a synergistic effect in reducing demineralisation on sound dentine in the laboratory. However, in situ situations are more complicated where no additive benefit was found by combining an APF gel with CO_2 laser irradiation in controlling RCL.[24] Nevertheless, a clinical case report demonstrated the potential of complementing the respective effectiveness of fluoride and CO_2 laser by combined application.[103]

1.6.2 Free Electron Laser (FEL)

A tuneable mid-infrared free electron laser (MIR-FEL) has been proposed for surface modification of root dentine and the extent of modification by varying wavelengths and average power has been investigated macroscopically.[104] Irradiated with MIR-FEL of λ = 9.0 or 9.7 μm, dentine surfaces exhibited increased acid resistance.[97]

1.6.3 Erbium, chromium: yttrium-scandium-gallium-garnet (Er, Cr:YSGG) laser

Er, Cr:YSGG laser with a wavelength of 2.78 μm is usually applied for cavity preparation due to the mechanism of ablation. Lasers with lower energy densities may not ablate the treated surface but change the tissue morphologically or chemically, thus being used for preventive purposes. This viewpoint was confirmed by an atomic force microscopy study that Er, Cr:YSGG laser at a low-energy density parameter can significantly alter the micro-topography of radicular dentine.[100] A significant synergistic effect of Er, Cr:YSGG laser associated with 2% neutral NaF application was demonstrated in increasing acid resistance of human root dentine.[101]

2 Methods to model root caries

Natural dentinal caries is complex with variations in width, depth, severity and colour, thus it is difficult to find similar lesions for laboratory studies. An artificial caries model system offers significant advantages over natural lesions for its consistency and reproducibility in the research for non-invasive treatment.

Van Dijk et al. presented a mathematical model to obtain an artificially caries-like lesion in 1979, which was followed by ten Cate et al. to produce artificial enamel lesions.[105, 106] Later, Xie et al. used the same method to produce artificial RCL.[76] In detail, demineralisation was carried out in solutions under-saturated with respect to hydroxyapatite, with a pH ranging from 4.4 to 5.0, for a time ranging from 16 h[26] to 5 d.[35, 77, 107] Accordingly, caries-like lesions were created with depths of 70 to 100 μm.[35, 77, 80, 76] Although without bacteria or enzymes present, the chemical model systems could create lesions with remarkable histological similarities (especially the mineral content and hardness) to natural RCL of similar depths.[108]

However, as organic acids produced by cariogenic lactobacilli are considered to play a major role in dentine demineralisation, another artificial dentine caries model based on lactate buffers has been proposed. Different acids yielded lesions with different characteristics that may impact on strategies for remineralisation.[109]

In addition to the above static method to create artificial lesions, pH-cycling models have been employed to mimic the dynamics of mineral loss and gain in carious lesion formation in the oral environment by exposing dental substrates to both demineralising and remineralising solutions. The exposure time in both solutions and the concentrations of the ions can be varied according to the purpose of the study. The duration of the whole process varies from 18 h to 14 d.[74, 82, 110, 111] The demineralisation periods were even divided into two 3 h demineralisation periods to more accurately simulate the time-per-day that teeth in the oral cavity would be exposed to the cariogenic challenge associated with meals.[43]

However, pH-cycling is a chemical model that is not able to estimate the antimicrobial effect of treatment substances on lesion progression or regression. Therefore, biofilm models have been created by using microbial inoculation for biofilm growth on root dentine specimens that forms carious lesions. However, controversy exists regarding how the biofilm is predominantly formed and the microbial diversity. Specifically, highly acidogenic and aciduric bacteria such as S. mutans and L. casei have been considered important in the aetiology of root caries and adopted as the microbial source for biofilm growth on root dentine slabs.[55, 112] However, there are other organisms involved in natural RCL development. Accordingly, a consortium plaque biofilm composed of four species, i.e. S. mutans, S. sobrinus, A. naeslundii, and L. rhamnosus, was constructed as a root caries model system.[91, 113] Although after incubation, the root dentine fragments showed alterations similar to that of root caries, the complex dental biofilm which consists of hundreds of bacterial species is difficult to simulate in a laboratory. Therefore, laboratory root caries models are often based on consortium biofilms of selected species of bacteria.[112-114]

The complexity of the oral environment led to the development of sophisticated ‘artificial mouth’ systems that simulate the oral environment humidity, temperature, and salivary characteristics and flow as well as providing a continuous or intermittent supply of nutrients to the biofilm.[115] The sophisticated model was also used for root caries research by Mei et al.,[89] where mixed salivary bacteria from individuals were obtained to form a microcosm and used to inoculate the root samples in the artificial mouth.

Removable intraoral palatal appliances containing dentine specimens have been used in some in situ studies, which are worn by volunteers. In this case, the root dentine samples are placed in the oral environment with the patients’ own bacteria to colonize specimens.[22, 24, 26, 28, 90]

Laboratory models are simple, low cost, fast and reproducible, and are indispensable for evaluating the effects of different treatment methods for RCL. However, they cannot fully replicate the multifactorial nature of root caries in the oral environment and clinical trials are still required among multiple patients and variable oral conditions to draw valid conclusions.

3 Restorative treatment

When the attempt to halt the progression of a RCL has failed and the lesion has advanced to frank cavitation, restorative treatment is then required. Restoration of RCL condemns the tooth to a repeat restoration cycle and therefore efforts are made to explore the MID approach. Also, challenges exist regarding new RCL formation associated with restorations as well as the failure rates of restorations.

Concerning restorative treatment for RCL, improvements have been made in the aspects such as novel techniques in carious tissue excavation and modification of restorative materials and procedures. Three clinical trials investigated the clinical outcomes of Atraumatic Restorative Treatment (ART) restorations.[29, 116, 117] Four studies analysed the efficacy of lasers (CO_2 and Er, Cr: YSGG) for carious tissue excavation.[118-121] Modification of restorative materials (such as adhesives, GIC and RC) or improvement in restorative procedure were investigated in seven laboratory studies.[122-126]

3.1 Techniques in carious tissue excavation

The conventional carious tissue excavation technique with rotary instrumentation has often resulted in considerable removal of tooth structure and extensive tissue loss, which is now considered to be overly destructive.[127] Also, it is not so feasible for use in some elders with physical or cognitive disorders as well as institutionalised patients, as they may not be able to visit a dental office.

3.1.1 Atraumatic Restorative Treatment (ART)

In light of the prevalent concept of MID, Atraumatic Restorative Treatment (ART) is a potential restorative technique for RCL management. It removes the completely necrotic carious tooth tissue with hand instruments while conserving the partially demineralised dentine. A restoration is then placed using an adhesive restorative material (usually GIC), which restores the cavity and seals any susceptible surfaces simultaneously. This could be more acceptable and accessible to frail elderly or nursing home residents than ‘conventional’ dental treatment.[128]

The survival rates of ART restorations have been compared with that of conventional rotary technique for periods of 6 months to 2 y, where the majority (>80%) of restorations were placed on one root surface only. Although significantly more failures could be observed in the ART than in the rotary technique, partly due to material failure, the success and survival rate were still high.[29, 116] As the removal of softened demineralised dentine by hand instruments may present challenges to the clinician in the elderly, a chemomechanical method using Carisolv® gel (Medi Team Dental AB, Sweden), which is composed of sodium hypochlorite and three amino acids - glutamic acid, leucine and lysine, and applied to assist the removal of denatured dentine compensating for the limitations of manual removal. However, the use of Carisolv® gel did not improve the success rate of GIC restorations used with ART technique in root caries of a geriatric population.[117] Admittedly, the failure of ART is associated with many factors, which include the restorative material used, operator, technique as well as oral health status of the patient. Still, ART is useful for outreach dental services, and warrants further investigation.

3.1.2 Lasers

Laser systems can be used for carious tissue removal and cavity preparation, which has been an area of major research interest. The efficacy of lasers depends on numerous factors that include the wavelength characteristics, pulse energy and repetition rate. Er, Cr:YSGG laser is favoured in minimally invasive procedures, especially for the preparation of microcavities, although the need for such restorations to be undertaken has been challenged recently.[129] A cavity prepared by Er, Cr:YSGG laser provided the lowest microleakage after GIC restoration compared with that prepared by a carbide bur at low speed or by hand excavator. Possible explanation is that the heat generated during laser irradiation increased the amount of calcium in the dentine substrate which in turn improved adhesion of the GIC.[124] However, the improvement in microleakage prevention was not observed in RC restorations.[119]

3.2 Improvement of restorative materials and procedures

Management of RCL with restorative materials such as GIC, RC and amalgam can be time-consuming and intractable because of the concomitant problems, such as difficulty in moisture control, poor marginal adaptation and proximity to the pulp, which can lead to leakage, new carious lesions at the restorative margins and finally restoration replacement or tooth failure. Hence, there is an urgent need to evolve restorative materials and procedures.

Glass-ionomer cement seems particularly suitable for restoring RCL. The major advantage of GIC is its ability for chemical bonding to tooth structure, act as a F^- reservoir in the oral cavity and possess acceptable aesthetic qualities and biocompatibility. It was shown to confer a preventive effect against cariogenic challenge by a mixed-species oral biofilm in an artificial mouth culture system.[130] Various modifications have been made in GIC composition to improve its properties, such as addition of CPP-ACP (Fuji VII EP; GC Corp., Tokyo, Japan) or enhancing fluoride release (Fuji IX GP; GC Corp., Tokyo, Japan).[131] Specifically, approximal RCL were restored with Fuji IX GP mean survival time of 74 months.[125, 132]

Resin composite has also been widely used for restoration of root surface caries as it does not require excessive removal of sound tooth structure. However, bacterial invasion (microleakage) could happen from the defective margin between RC and tooth structure if the environment continues to be cariogenic. An alternative means of clinical management to reduce this problem is to provide the restorative material with a therapeutic effect, such as incorporating antibacterial and remineralising components into the adhesive systems. The monomer, 12-methacryloyloxydodecylpyrinium bromide (MDPB), was developed by combining a quaternary ammonium group and a methacryloyl group into an adhesive system. The quaternary ammonium component presents a wide spectrum of antibacterial activity. The MDPB containing adhesive significantly reduced recurrent lesion formation around restorations, being a good candidate for restoring RCL.[122] Other novel multifunctional adhesives have been developed in the laboratory by adding substances with different activities. However, no clinical evaluation has occurred.[126] In addition, in the cases of deep cavities where restorative treatment is required, the intensity of the pulpal response should be considered and the thus use of liners have been evaluated. Resin-modified GIC (RMGIC) has been used as a lining material to protect the pulp from further bacterial invasion. Its application did not affect marginal adaptation and retention of restorations over an 18-month period.[123]

Another strategy proposed to optimise the longevity of restorations is to involve additional steps within the restorative procedure. A conjunctive use of 1.23% APF gel or 2.0% neutral NaF gel with GIC and RMGIC restorations inhibited the progression of caries-like lesions adjacent to restorations.[133] Additionally, CO_2 laser has been considered for inhibition of recurrent caries adjacent to restorations. Irradiation of cavo-surface margins of the prepared root surface with a λ 10.6 μm CO_2 laser at densities of 5.0 and 6.0 J/cm^2 reduced the demineralisation with the rates of 17.05% and 20.59% respectively around RC restorations.[118, 120] Its efficacy in GIC restorations was related to different GIC products used.[121]

Conclusion

In conclusion, this literature review summarised the various treatment approaches for RCL in the last decade. Non-invasive or invasive treatment methods were chosen according to the progression of RCL. Agents and substances applied in non-invasive methods involved fluoride containing products, cross-linkers, collagenase inhibitors and antibacterial agents. These agents mainly aimed at reducing demineralisation, promoting remineralisation and suppressing cariogenic microorganism growth. Dentine surface modification conducted by lasers increased resistance to RCL formation. Restorative treatment is necessary when RCL have advanced to frank cavitation with significant dental tissue loss. Improvements have been made regarding carious tissue excavation techniques and modifications of restorative materials and procedures. As invasive treatment with restorations is merely symptomatic in nature without dealing with the essential causative factors of dental caries. It is of importance to determine the most appropriate treatment for RCL. Clinical trials are urgently needed to draw firm conclusions concerning the efficacy of the various treatment methods described.

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Author, year	Intervention	Control	Type	Outcomes measured	Effects
Fluoride formulations					
Petersson, 2007[63]	1400 ppm FD + 250 ppm F mouthwash (Elmex ® Sensitive Plus, Colgate-Palmolive, USA). Twice/day	1400 ppm FD + placebo mouthwash, twice/day	Clinical trial	ECM; changes in surface texture	
Ekstrand, 2008[53]	1450 ppm FD twice/day + (Professionally) 1450 ppm FD (Colgate Palmolive, UK) & Duraphat varnish once/mouth	1450 ppm FD; 5000 ppm FD (Duraphat; Colgate-Palmolive, UK); twice/day	Clinical trial	Number of RCL	
Fure, 2009[57]	Carisolv® chemo-mechanical technique (Mediteam Savedalen, Sweden) + Duraphat 2.23% F varnish (Colgate-Palmolive, USA)	Duraphat 2.23% F varnish (Colgate-Palmolive, USA); SnF_2 solution (8%);	Clinical trial	DMFS; DFRS as a percentage of exposed root surfaces (DFRS %); CFU in plaque from RCL	
Vered, 2009[30]	Colgate® Total plus Whitening Toothpaste (0.243% NaF, 0.3% triclosan in a silica base) (Colgate-Palmolive, USA)	Colgate NaF toothpaste without triclosan	Clinical trial	Katz root caries index; mean RCL increment	
Jing, 2010[35]	Hydoxyapatite nanoparticle	1000 ppm F (NaF); DW	Laboratory study	Knoop hardness test	
Petersson, 2011[48]	5 ppm F-milk/probiotic bacteria	Standard milk (placebo); milk with probiotic bacteria; 5 ppm F milk	Clinical trial	ECM; mean RCL increment	
Ekstrand, 2013[42]	5000 ppm FD (Duraphat; Colgate Palmolive, UK) (professionally)	1450 ppm FD (Colgate Ultra Cavity Protection; Colgate Palmolive, UK) (professionally)	Clinical trial	Number of arrested/active RCL	Arrest and remineralisation of caries lesions

Hu, 2013[31]	1.5% arginine, 1450 ppm FD (sodium monofluorophosphate, calcium based) (Colgate-Palmolive, USA)	1450 ppm FD (NaF, silica based); non-FD (calcium based)	Clinical trial	Hardness change; ECM	
Souza, 2013[19]	1.5% arginine, 1450 ppm FD (sodium monofluorophosphate) (Colgate-Palmolive Company, Germany)	1450 ppm FD (sodium monofluorophosphate)	Clinical trial	Lesion size and distance from the gingival margin; texture change	
Goettsche, 2014[43]	5000 ppm FD (ClinPro 5000, 3M ESPE); CSPS toothpaste (ReNew, Sultan, Healthcare); Prevident 5000 gel (Colgate Oral Pharmaceuticals)	DW	Laboratory study	Mean depth of cavitation/remineralisation band/lesion	
Srinivasan, 2014[20]	1.1% NaF (5000 ppm F) FD (Duraphat, Colgate-Palmolive Company, Germany)	Standard regular FD (Odol-med 3, 1350 ppm F; GlaxoSmithKline, Bruhl, Germany).	Clinical trial	Hardness change	
Xin, 2016[18]	5% NaF varnish (Duraphat®, Colgate, Colgate-Palmolive Company, USA)	A water-based gel without F as placebo (K-Y® Gel, McNEIL-PPC Inc., Fort Washington, USA)	Clinical trial (Patients with Sjögren's syndrome)	Mean DMFT, mean arrested root caries, mean oral Candida counts	
Papas, 2008[34]	1100 ppm FD supplied with Ca^{2+}/PO_4^{3-} (Enamelon Inc., USA)	Conventional 1100 ppm FD	Clinical trial (Patients with head and neck radiation)	RCL increment per year	Reduction of root caries incidence/inhibition of caries
Singh, 2009[44]	Compliant patients using 1.1% NaF with neutral supersaturated Ca^{2+}/PO_4^{3-}	Non-compliant patients using the same intervention	Clinical trial (Patients with	Risk for caries (surface at risk)	progression and

	mouthrinse (Caphasol, EUSA Pharma, USA) at least once a day	less than once a day	Xerostomia)		demineralisation
Diamanti, 2010[33]	Toothpaste slurries with 7.5% CSPS/1450 ppm F/2800 ppm F/5000 ppm F	PD	Laboratory study	Knoop hardness test	
Vale, 2011[28]	APF gel (1.23% F, DENTSPLY, Brazil) +1100 ppm FD	PD, 1100 ppm FD, APF gel+ PD,	In situ trial	Surface hardness loss, integrated mineral loss, fluoride analysis in biofilm fluid and solids, determination of CaF_2 and FAp in dentine	
Giacaman, 2012[49]	5 ppm F bovine milk	0.9% NaCl; no F bovine milk; 0.05% NaF	Laboratory study (Bovine)	Biofilm measurement, surface hardness loss	
Garcia-Godoy, 2013[46]	Xylitol FD (1100 ppm sodium monofluorophosphate, 0.20% xylitol, Fisher Scientific, USA).	No treatment; 1150 ppm FD (Aquafresh® Advanced, GlaxoSmithKline, USA); Experimental xylitol PD (0.45% xylitol, LMKao LLC, USA);	Laboratory study	Mean lesion depth	
Arnold, 2014[51]	Whole milk 3.5% fat + 2.5 ppm/10 ppm fluoride	Whole milk 3.5% fat	Laboratory study	Lesion depth, elemental distribution	

Botelho, 2014[23]	1100 ppm FD (NaF, silica-based) (Colgate Palmolive, Brazil)	PD	Laboratory study (Bovine)	Surface hardness loss
Garcia-Godoy, 2014[41]	Denticious 5000 FD (5000 ppm F + xylitol, Research Based Professional Products, USA); PreviDent® 5000 dentifrice (5000 ppm F, Colgate-Palmolive, USA); AIM® dentifrice (1500 ppm F, Church & Dwight, USA); Listerine® dentifrice (1300 ppm F, Johnson & Johnson, USA); Crest® Regular Paste (1500 ppm F, Procter & Gamble, USA).	No treatment	Laboratory study	Mean lesion depth
Arthur, 2015[54]	1450 ppm FD (twice/day) + 226 ppm F mouthwash (Colgate Plax) (once/day);	DW (3 times/day); 1450 ppm FD (Colgate Total) (twice/day); 1450 ppm FD (3 times/day)	Laboratory study (Bovine)	Lesion depth, integrated mineral loss, Knoop hardness test
Katsura, 2016[32]	10 % CPP-ACP paste (GC Corporation, Japan) with NaF toothpaste	NaF toothpaste alone, non-CPP-ACP	Clinical trial (patients with head and neck radiotherapy)	Surface texture change
Magalhaes, 2016[60]	TiF_4/NaF solution (500 ppm F, pH 4.4); NaF varnish (24 500 ppm F, pH 5.0); TiF_4 varnish (24 500 ppm F, pH 1.0); TiF_4 varnish + TiF_4/NaF solution; NaF varnish +	No treatment	Laboratory study (Bovine)	Mineral loss; tooth erosion

	TiF_4/NaF solution				
Nobrega, 2016[26]	1100 ppm FD (Colgate-Palmolive, Brazil), 1, 2, or 3 times/day	PD	Laboratory study (Bovine)	Surface hardness loss	
Thanatvarakorn, 2016[61]	4.18% ZnF_2•$4H_2O$ in HCl (F=9048 ppm, Zn=1.56%, pH 2.7); 4.18% ZnF_2•$4H_2O$ (partially dissolved; F=9048 ppm, Zn=1.56%)	SDF (Saforide, Bee Brand Medico Dental, Osaka, Japan; 44 880 ppm F, 25.5% Ag+); Potassium fluoride (44 880 ppm F, neutral pH); APF (NaF in 0.1 M H_3PO_4; 9048 ppm F, pH 3.8); no F treatment.	Laboratory study (Bovine)	Lesion depth, mineral loss, collagen degradation (erosion depth)	
Fernandez, 2017[25]	APF gel (12 300 ppm F, pH 3.6-3.9; DFL, Petropolis, Brazil) +1100 ppm FD	PD; 5000 ppm FD (NaF/silica, Colgate-Palmolive, Brazil)	Laboratory study (Bovine)	Cross-sectional hardness; loosely/firmly bound fluoride concentration	
Commercialised available fluoridated sealants used for root caries prevention					
Gernhardt, 2007[27]	Sybtac Classic (Vivadent, Liechtenstein) and Xeno III (DENTSPLY, Germany) dentine bonding agents; Hyposen (lege artis, Germany) desensitizer.	No treatment	Laboratory study	Lesion depth	
Daneshmehr, 2008[65]	(F-releasing adhesives) Reactmer Bond (Shofu Inc., Japan) and Shake One (Shofu Inc., Japan)	(Non F-releasing adhesive) Hybrid Bond (Sun Medical, Moriyama, Japan)	Laboratory study (Bovine)	Biofilm measurement	Reduction of root caries incidence/inhib

Walter, 2008[82]	(Adhesive systems) Gluma Comfort Bond + Desensitizer (Heraeus Kulzer, Germany); Gluma Comfort Bond (Heraeus Kulzer, Germany); iBond (Heraeus Kulzer, Germany); One-up Bond F (Tokuyama, Japan)	No treatment or etched with 37% phosphoric acid	Laboratory study (Bovine)	Lesion depth	ition of caries progression and demineralisatio n
Shiiya, 2012[69]	F-releasing varnish containing surface reaction-type prereacted glass-ionomer (S-PRG) fillers (Shofu Inc., Japan)	An S-PRG filler-free varnish	Laboratory study (Bovine)	Mineral profiles, integrated mineral loss, lesion depth	
Sohn, 2012[66]	(F-containing desensitizers) Clinpro XT Varnish (3M ESPS); Seal & Protect (DENTSPLY, Germany); Clearfil Protect Bond (Kuraray, Japan)	No treatment	Laboratory study	Lesion depth, Calcium loss,	
Oshima, 2015[67]	MS Coat One (containing methacrylate-co-p-styrene sulfonic acid (MS polymer) and 1% oxalic acid); MS Coat F (containing MS polymer, 1% oxalic acid and 3000 ppm sodium fluoride)	No treatment; 1% oxalic acid	Laboratory study (Bovine)	Mineral loss	
Miyajima, 2016[68]	Calcium-fluoroaluminosilicate glass-based desensitizer (Nano Seal, Prevest DenPro, India)	No treatment	Laboratory study	Mineral loss, lesion depth	
Cross-linkers					
Walter, 2008[133]	0.5% proanthocyanidin (PA); 0.625% genipin	5% glutaraldehyde (GA)	Laboratory study (Bovine)	Lesion depth; root surface colonization	Reducing demineralisatio

Xie, 2008[75]	6.5% grape seed extract (GSE)	No treatment; 1000 ppm F (NaF);	Laboratory study	Knoop hardness test; mineral precipitation profiles	n and with the potential to
Hiraishi, 2011[73]	10 ppm, 100 ppm, 1000 ppm, 10 000 ppm hesperidin (Wako Pure Chemical Industries, Ltd., Tokyo, Japan)	2000 ppm CHX (Sigma–Aldrich, St. Louis, MO, USA)	Laboratory study (Bovine)	Collagen degradation (calcium release); lesion depth; mineral loss	promote remineralisatio n
Pavan, 2011[109]	6.5% GSE + 1000 ppm F	DW; 6.5% GSE; 1000 ppm F	Laboratory study	Lesion depth; mineral loss; collagen degradation depth	
Benjamin, 2012[76]	6.5% GSE	No treatment; Sodium monofluorophosphate (220 ppm) with 0.05% calcium glycerophosphate or 0.5% calcium glycerophosphate	Laboratory study	Relative optical density	
Guo, 2012[77]	4000 mg/L Galla chinensis extract	Artificial saliva; DW	Laboratory study (Bovine)	Lesion depth	
Islam, 2012[74]	0.5% hesperidin (Wako Pure Chemical Industries, Ltd., Tokyo, Japan); 0.5% GSE (Gravinol® grape seed extract, Kikkoman, Chiba, Japan)	0.2% CHX (Sigma-Aldrich, St. Louis, MO, USA)	Laboratory study	Lesion depth, mineral loss	
Tang, 2013[134]	5%, 10%, 15% GSE (acidic and neutralized)	DW	Laboratory study	Vickers hardness test	
Epasinghe,	6.5% PA + CPP-ACFP paste	6.5% PA; CPP-ACP paste; CPP-ACFP	Laboratory study	Lesion depth, mineral loss, Knoop hardness test	

2015[81]		paste; 1000 ppm F; DW			
Epasinghe, 2016[79]	6.5% PA; 6.5% naringin; 6.5% quercetin	1000 ppm F; DW	Laboratory study	Lesion depth, mineral loss, Knoop hardness test	
Epasinghe, 2017[80]	6.5% PA + tri-calcium phosphate (TCP) + F	6.5% PA; TCP + F; 1000 ppm F; DW	Laboratory study	Lesion depth, mineral loss, Knoop hardness test	
MMP inhibitors					
Fukuda, 2009[83]	0.042%; 0.083%; 0.167%; 0.330% piroctone olamine (PO)	0.07% NaF	Laboratory study (Bovine)	Lesion depth, mineral loss	Inhibition of mineralisation
Hannas, 2016[78]	0.61% green tea extract; 0.12% or 0.004% CHX	PD; 1100 ppm F	Laboratory study	Mineral loss	
Antimicrobial treatments					
Baca, 2009[91]	1% CHX - 1% thymol (Cervitec® varnish, Vivadent, Liechtenstein)	A placebo varnish	Clinical trial	Plaque index, gingival index, DFT, root caries index, oral biofilms levels); RCL incidence; lesion size; changes in texture/colour	Arrest and remineralisation of caries lesions
Bizhang, 2015[22]	1% CHX -1% thymol (Cervitec plus®, Ivoclar Vivadent, Liechtenstein); 10% F^- (Bifluoride 10®, VOCO GmbH, Cuxhaven, Germany)	No treatment	In situ trial	Integrated mineral loss, lesion depth	
Zheng,	0.2% CHX (Corsodyl, SmithKline Beecham	DW	Laboratory study	CFU	Antibacterial

2011[90]	Consumer Healthcare, UK); Listerine (IDS Manufacturing, Thailand); Fluoride Listerine (IDS Manufacturing, Thailand).				effects, prevention of caries
Rolland, 2011[92]	Clearfil SE Bond (SE; Kuraray Medical, Japan; MDBP-containing resins as sealants);	Clearfil Protect Bond (PB; Kuraray Medical)	Laboratory study	Total CFU and percentage reduction in CFU	
Mei, 2013[88]	0.12% CHX	DW	Laboratory study	CFU; LIVE/DEAD BacLight Bacterial Viability; mineral/organic content	
Tan, 2010[87]	Oral hygiene instruction (OHI) + 38% SDF solution (Saforide, Toyo Seiyaku Kasei Co. Ltd., Japan)	OHI; OHI + 1% CHX varnish; OHI + 5% NaF varnish	Clinical trial	Mean number of RCL	Prevention and arrest of caries
Zhang, 2013[16]	38% SDF (Saforide, Toyo Seiyaku Kasei Co. Ltd., Japan) + Oral hygiene instruction (OHI) + Oral health education (OHE)	OHI; OHI + 38% SDF	Clinical trial	Exposed sound root surfaces; DFRS; arrested root surfaces; mean number of new/arrested root caries surfaces.	
Li, 2016[17]	38% SDF solution (Saforide, Toyo Seiyaku Kasei Co., Ltd., Japan); 38% SDF solution + KI solution (2.36 mol/L)	Placebo (soda water with a bitter flavour)	Clinical trial	Mean number of exposed sound root surface/DFRS/active decayed root surfaces; arrest rates of baseline active caries.	
Baysan, 2007[93]	Ozone (HealOzone, KaVo Dental GmbH, Germany) + root sealant (Seal & Protect, Dentsply International, UK);	No treatment control; ozone; root sealant	Clinical trial	ECM, DIAGNOdent device, clinical assessment (colour, hardness, cavitation, dimensions, distance from the gingival margin,	Reversal of leathery root caries

				and severity index)	
Van Strijp, 2008[89]	0.2% CHX mouthrinse (Corsodyl; GlaxoSmithKline, The Netherlands)	Saline (0.9% NaCl) mouthrinse	In situ trial	Integrated mineral loss; lesion depth; lactic acid analyses	Prevention of demineralisation
Lasers					
Heya, 2008[96]	Mid-infrared Free Electron laser (9.0 or 9.7 µm)	No treatment	Laboratory study	Morphological and chemical changes	Prevention of caries
De souza-Zaroni, 2010[101]	10.6 µm CO_2 laser (2.5 J/cm^2; 4.0 J/cm^2; 5.0 J/cm^2; 6.0 J/cm^2 per shot) (UM-L30, Union Medical Engineering Co., Yangju-si, Gyeongii-Do, Korea)	No treatment	Laboratory study	Mineral loss, morphology	
Parisotto, 2010[135]	CO_2 laser (10.6 µm) (UM-L30, Union Medical Engineering Co., Yangju-si, Gyeongii, Korea) + Acidulated phosphate fluoride (APF) gel (1.23% F, pH=3.6-3.9, Dfl Industria E Comercio S.A., Brazil)	No treatment; 1.23% APF gel; CO_2 Laser	Laboratory study (Bovine)	Knoop hardness test	
Colucci, 2012[24]	CO_2 laser (10.6 µm, 6.25 J/cm^2) (PC015D, Shanghai Jue Hua Laser Technolgy Development Co., China) + 1.23% APF gel (Bioquanti, Brazil)	No treatment; 1.23% APF gel; CO_2 laser	In situ trial	Knoop hardness test	
Esteves-Oliveira,	CO_2 laser (10.6 mm, 8 or 11 J/cm^2) (UM-L30, Union Medical Engineering Co., USA) with or without 1.23% acidulated phosphate fluoride (APF) gel (DFL Ltd., Rio de	No treatment; APF gel	Laboratory study (Bovine)	Calcium and phosphorous contents released in the de- and remineralisation solution	

2011[98]	Janeiro, Brazil)			
Geraldo, 2014[100]	Er, Cr: YSGG laser (4.64 or 8.92 J/cm2) (WaterLase Millennium™, Biolase Inc., USA) with or without 2% neutral NaF gel (Colorama Maybelline Ltd., Brazil) with or without water cooling (5.4 mL/min);	No treatment; 2% NaF gel	Laboratory study	Knoop hardness test

CFU = colony forming units; CHX = chlorhexidine; CSPS = calcium sodium phosphosilicate; DFRS = decayed and filled root surfaces; DFT = decayed and filled teeth; DMFS = decayed, missed and filled surfaces; ECM = electrical caries monitor; FD = fluoride dentifrice; NaF = sodium fluoride; PD = placebo dentifrice; RCL = root caries lesions; SnF_2 = stannous fluoride; TiF_4 = titanium fluoride.

Table 1 Categorisation of non-invasive treatment for root caries

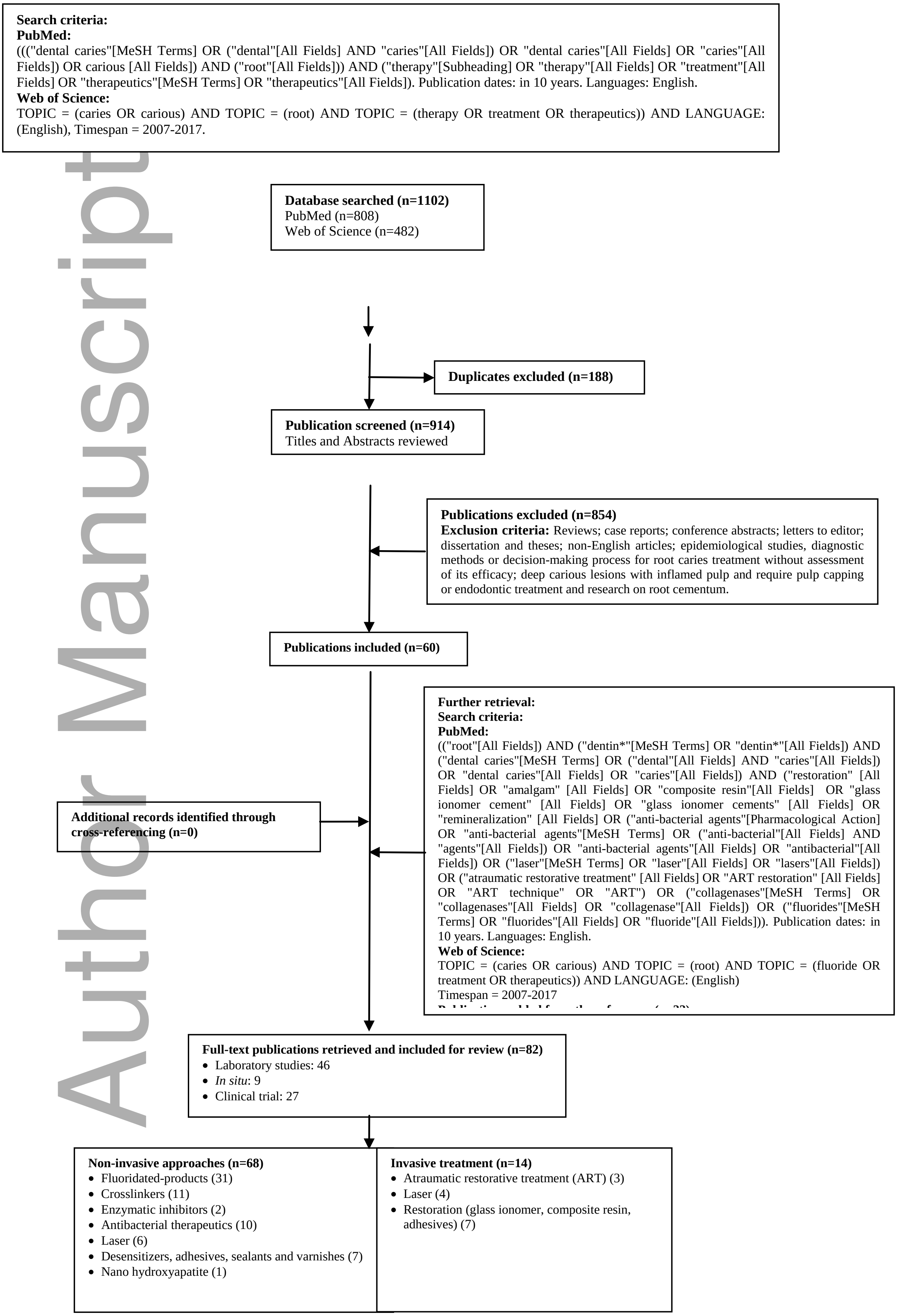
Search criteria:
PubMed:
((("dental caries"[MeSH Terms] OR ("dental"[All Fields] AND "caries"[All Fields]) OR "dental caries"[All Fields] OR "caries"[All Fields]) OR carious [All Fields]) AND ("root"[All Fields])) AND ("therapy"[Subheading] OR "therapy"[All Fields] OR "treatment"[All Fields] OR "therapeutics"[MeSH Terms] OR "therapeutics"[All Fields]). Publication dates: in 10 years. Languages: English.
Web of Science:
TOPIC = (caries OR carious) AND TOPIC = (root) AND TOPIC = (therapy OR treatment OR therapeutics)) AND LANGUAGE: (English), Timespan = 2007-2017.
Database searched (n=1102)
PubMed (n=808)
Web of Science (n=482)
Duplicates excluded (n=188)
Publication screened (n=914)
Titles and Abstracts reviewed
Publications excluded (n=854)
Exclusion criteria: Reviews; case reports; conference abstracts; letters to editor; dissertation and theses; non-English articles; epidemiological studies, diagnostic methods or decision-making process for root caries treatment without assessment of its efficacy; deep carious lesions with inflamed pulp and require pulp capping or endodontic treatment and research on root cementum.
Publications included (n=60)
Further retrieval:
Search criteria:
PubMed:
(("root"[All Fields]) AND ("dentin*"[MeSH Terms] OR "dentin*"[All Fields]) AND ("dental caries"[MeSH Terms] OR ("dental"[All Fields] AND "caries"[All Fields]) OR "dental caries"[All Fields] OR "caries"[All Fields]) AND ("restoration" [All Fields] OR "amalgam" [All Fields] OR "composite resin"[All Fields] OR "glass ionomer cement" [All Fields] OR "glass ionomer cements" [All Fields] OR "remineralization" [All Fields] OR ("anti-bacterial agents"[Pharmacological Action] OR "anti-bacterial agents"[MeSH Terms] OR ("anti-bacterial"[All Fields] AND "agents"[All Fields]) OR "anti-bacterial agents"[All Fields] OR "antibacterial"[All Fields]) OR ("laser"[MeSH Terms] OR "laser"[All Fields] OR "lasers"[All Fields]) OR ("atraumatic restorative treatment" [All Fields] OR "ART restoration" [All Fields] OR "ART technique" OR "ART") OR ("collagenases"[MeSH Terms] OR "collagenases"[All Fields] OR "collagenase"[All Fields]) OR ("fluorides"[MeSH Terms] OR "fluorides"[All Fields] OR "fluoride"[All Fields])). Publication dates: in 10 years. Languages: English.
Web of Science:
TOPIC = (caries OR carious) AND TOPIC = (root) AND TOPIC = (fluoride OR treatment OR therapeutics)) AND LANGUAGE: (English)
Timespan = 2007-2017
Additional records identified through cross-referencing (n=0)
Full-text publications retrieved and included for review (n=82)
Laboratory studies: 46
In situ: 9
Clinical trial: 27
Non-invasive approaches (n=68)
Fluoridated-products (31)
Crosslinkers (11)
Enzymatic inhibitors (2)
Antibacterial therapeutics (10)
Laser (6)
Desensitizers, adhesives, sealants and varnishes (7)
Nano hydroxyapatite (1)
Invasive treatment (n=14)
Atraumatic restorative treatment (ART) (3)
Laser (4)
Restoration (glass ionomer, composite resin, adhesives) (7)

Figure 1 Flowchart of search strategy.