Japanese Dental Science Review 58 (2022) 249–257

Contents lists available at ScienceDirect

Japanese Dental Science Review

journal homepage: www.elsevier.com/locate/jdsr

Review article

Silver diamine fluoride therapy for dental care

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ARTICLE INFO

Article history:
Received 26 February 2022
Received in revised form 5 August 2022
Accepted 21 August 2022

Keywords:
Silver diamine fluoride
Caries
Prevention
Dentine
Hypersensitivity

ABSTRACT

Silver diamine fluoride (SDF) was developed in Japan in the 1960s. It is used to control early childhood caries, arrest root caries, prevent fissure caries and secondary caries, desensitise hypersensitive teeth, remineralise hypomineralised teeth, prevent dental erosion, detect carious tissue during excavation and manage infected root canals. SDF is commonly available as a 38% solution containing 255,000 ppm silver and 44,800 ppm fluoride ions. Silver is an antimicrobial and inhibits cariogenic biofilm. Fluoride promotes remineralisation and inhibits the demineralisation of teeth. SDF also inactivates proteolytic peptidases and inhibits dentine collagen degradation. It arrests caries without affecting dental pulp or causing dental fluorosis. Indirect pulp capping with SDF causes no or mild inflammatory pulpal response. However, direct application of SDF to dental pulp causes pulp necrosis. Furthermore, SDF stains carious lesions black. Patients must be well informed before SDF treatment. SDF therapy is simple, painless, non-invasive, inexpensive, and requires a simple armamentarium and minimal support. Both clinicians and patients generally accept it well. In 2021, the World Health Organization included SDF as an essential medicine that is effective and safe for patients. Moreover, it can be used for caries control during the COVID-19 pandemic because it is non-aerosol-generating and has a low risk of cross-infection.

Contents

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https://doi.org/10.1016/j.jdsr.2022.08.001

1. Introduction

For many years, dentists in countries such as Argentina, Australia, Brazil, China and Japan have used silver diamine fluoride (SDF) as an anti-caries agent [1]. It is effective in arresting cavitated dentine carious lesions and preventing new caries development [2]. SDF is used to arrest early childhood caries [3], manage root caries [4], prevent pit and fissure caries [5], impede secondary caries [6], remineralise hypomineralised teeth [7], treat infected root canals [8] and desensitise hypersensitive teeth [9]. Some clinicians have suggested using SDF to manage dental erosion [10]. Other clinicians have suggested using SDF as a detecting dye for carious tissues to guide caries excavation [11]. Researchers have applied laser irradiation with SDF therapy to prevent tooth fracture after endodontic treatment [12] and to prevent root caries development by increasing fluoride uptake in dentine [13,14].

Rosenblatt and co-workers called SDF a silver-fluoride bullet for caries management because SDF is a safe, effective, efficient and equitable caries control agent [15]. They concluded that SDF may meet the criteria of caries treatment of the United States Institute of Medicine and the World Health Organization (WHO) Millennium Development Goals. In 2021, the WHO included SDF as one of the most efficacious, safe and cost-effective medicines for meeting the most important needs in a health system for adults and children [16]. Considering the growing evidence of successful SDF therapy, it has become a popular clinical treatment in recent years. A survey in the United States found that paediatric dentistry residency programmes had universally adopted SDF for arresting caries in 2020, but only a quarter (26%) of them reported using SDF in 2015 [17]. SDF has also attracted researchers' attention since 2016. A recent bibliometric analysis found that global research interest regarding SDF increased exponentially in the five years from 2016 to 2021 [18]. Furthermore, there has been a steady increase in scientific research on SDF, which has been translated into clinical practice to improve the quality of dental care. The objective of this review paper is to provide an overview of SDF use in dentistry.

2. History of SDF use in different countries

Professor Misuho Nishino at Osaka University formulated a 38% SDF solution during her PhD studies in the 1960s [19]. She and her supervisor, Professor Reichi Yamaga, reported the clinical applications of SDF in 1972 [6]. The Central Pharmaceutical Council of Japan's Ministry of Health and Welfare accepted SDF as a therapeutic agent for dental treatment [3]. It is manufactured in Japan as a 38% SDF solution and a 3.8% SDF solution, which are marketed as Saforide and Saforide RC, respectively, for dental treatment.

In China, Professor YJ Li at Beijing Capital Medical University developed a low-cost 38% SDF solution for arresting caries. She reported the effectiveness of SDF in arresting caries in 1984 [20]. Dentists in some hospitals also used SDF to treat dentine hypersensitivity [9]. However, the use of SDF became unpopular in China, probably because dentists could not charge for caries-arresting treatment with SDF. Few publications regarding SDF can be found in the literature before 2000 [21,22]. In 2002, a research team searched for alternative treatments for caries management. Based on a PhD study, they found that SDF could arrest caries without excavating the soft, active carious tissue [23]. The research team subsequently conducted several seminal laboratory studies [24–29] and clinical trials [30–35], which have contributed to an understanding of caries arrest using SDF. In 2019, Professor C H Chu at the University of Hong Kong implemented a dental outreach service programme using SDF to arrest dental caries to preschool children. All the 180,000 kindergarten children were eligible to receive SDF therapy with parental consent in their kindergartens.

In Australia, Dr Graham Graig at the University of Sydney used 40% neutral silver fluoride solution to treat caries. He reported the silver fluoride solution could slow down caries in primary teeth in 1980s [36]. The Western Australia School Dental Service used silver fluoride solution to arrest caries of school children. Because the silver fluoride-stained caries black, Dr Geoffrey Knight in the 2000s at the University of Adelaide used potassium iodide to remove the black staining [37]. A manufacturer subsequently developed SDF with potassium iodide (Riva Star). Although Riva Star was approved as a tooth desensitising agent in Australia, dentists use it to treat dental caries.

In the United States, Professor Peter Milgrom at University of Washington studied SDF for management of dental caries and dentine hypersensitivity [38,39]. In 2014, the United States Food and Drug Administration cleared the use of SDF for dentine desensitisation in adults over 21 years of age. Since 2015, SDF has been manufactured in the United States as a 38% solution. It is commercially available as Advantage Arrest as an anti-hypersensitivity agent for dental treatment, and many dentists use SDF for caries treatment. In 2016, the United States Food and Drug Administration granted the manufacturer breakthrough therapy status as part of the process of seeking approval for SDF as a drug formally indicated for arresting dental caries. In 2017, Health Canada approved the use of a product of SDF (Advantage Arrest) for caries treatment. An implementation research team partnered with the First Nations Health and Social Secretariat of Manitoba and the Manitoba Metis Federation to use SDF for management of early childhood caries in indigenous communities in Manitoba, Canada [40]. In addition, several other Indian Health Service and tribal programs in Alaska now use SDF for caries management with promising results [41].

In Cambodia, Professor Durward at the University of Puthisastra and Dr Turton conducted the Healthy Kids Cambodia project in 2016 [42]. The aim of the project is to provide a sustainable and integrated approach to primary health care for school children in Cambodia. The project incorporated the use of SDF as an essential treatment intervention to achieve universal oral health care [43]. The participated children received 30% SDF (Cariestop) to arrest dental caries on their primary teeth after screening.

In Thailand, the Dental Association of Thailand launched a guideline for fluoride usage including SDF. In 2018, the Thailand Food & Drug Administration approved a commercial product of 38% SDF (Topamine) for treatment of dentine hypersensitivity. The Ministry of Public Health Thailand subsequently approved SDF for treatment of coronal caries in primary teeth and root caries in permanent teeth. Dentists can use SDF as a professional fluoride therapy which is covered by the Universal Health Coverage in Thailand.

In 2020, the American Dental Association supported the use of SDF for caries management [44]. A national billing code (D1354) exists for dentists in the United States to use to charge for SDF therapy. Another billing code (D1355) was approved to SDF for caries prevention. Moreover, government and private insurance programmes cover SDF therapy for dental care. The American Medical Association is considering a Current Procedural Terminology (CPT) code for SDF therapy. The CPT is a standardised code set to report medical services and procedures to physicians, insurance companies and accreditation organisations.

In 2021, the WHO included SDF in the WHO Model List of Essential Medicines for both adults and children [16]. The WHO considers that SDF is a medicine to which everyone should always have access and that all governments should ensure SDF is available and affordable to their populations. Unfortunately, SDF is not yet available in all countries. Although government organisations and dental associations have developed guidelines for clinical use of SDF [1], some countries have no guidelines for SDF use. Table 1 shows guidelines and current usage of SDF in some countries. Because SDF is not available in some countries, dentists use silver nitrate solution first, then apply sodium fluoride varnish to arrest dental caries [45].

Several manufacturers have developed and marketed SDF solutions with various concentrations for dental use (Table 2). SDF is generally used as a 38% solution for treating caries and dentine hypersensitivity. Studies have found that SDF is significantly less effective in arresting caries at a low concentration (10–12%) than that at a high concentration (38%) [34,61]. A manufacturer has developed 3.8% SDF solution (Saforide RC, Toyo Seiyaku Kasei Co. Ltd., Osaka, Japan) as a disinfection agent for root canal therapy.

Table 1
Countries and guidelines for silver diamine fluoride (SDF) use *(adapted from Gao et al., 2021 [1])*.

Countries	Guidelines for SDF use (Reference number)
Africa	
Egypt	No
Ghana	No
Kenya	No
Nigeria	No
South Africa	No
Asia	
India	No
Japan	Clinical practice guideline for caries treatment [46]
Mongolia	Standard guidance and recommendation for SDF [45]
Thailand	Guideline on caries diagnosis and management [47]
Europe	
Finland	National guidelines for caries management [48]
Switzerland	Clinical guidance and recommendation for caries management [49–52]
United Kingdom	• Standard operating procedure (England) [53] • New SDF resources by the British Society of Paediatric Dentistry [54]
North America	
Canada	New guidance in treating caries by the Canadian Dental Association [55]
United States	• Guidelines for SDF use by the American Academy of Pediatric Dentistry[56] • Evidence-based clinical practice guideline on nonrestorative treatments for carious lesions by the American Dental Association [57]
South America	
Argentina	No *(Individual organisations have their own recommendations)*
Brazil	• National protocol in primary health care for the Brazilian public health system [58] • Guidelines for clinical procedures in paediatric dentistry [59]
Oceania	
Australia	Australian fluoride guidelines [60]

Table 2
Concentrations of some commercially available SDF solutions for dental use.

SDF%	Product	Manufacturer	Country
38%	Advantage Arrest	Elevate Oral Care	US
38%	Bioride	DENTSPLY Industrial & Commercial Ltd.	Brazil
38%	e-SDF	Kids-e-Dental	India
38%	Dengen Caries Arrest	Dengen Dental	India
38%	Fagamin	Tedequim SRL	Argentina
38%	Fluoroplat	NAF Laboratory	Argentina
38%	Riva Star	SDI Dental Ltd.	Australia
38%	Saforide	Toyo Seiyaku Kasei Co. Ltd.	Japan
38%	Topamine	Dentalife Australia Pty. Ltd.	Thailand
30%	Ancárie	Maquira, Maringá	Brazil
30%	Cariestop	Biodinamica	Brazil
12%	Ancárie	Maquira, Maringá	Brazil
12%	Cariestop	Biodinamica	Brazil
10%	Cariestatic	Inodon Dentistry	Brazil
3.8%	Saforide RC[a]	Toyo Seiyaku Kasei Co. Ltd.	Japan

[a] For root canal therapy

3. Ingredients and concentrations of SDF solution

SDF is a colourless alkaline solution with a pH value between 9 and 10. It can be tinted blue to facilitate SDF application. Although the manufacturers have not disclosed details about the ingredients [62], their SDF products basically contain silver, fluoride and ammonia. Silver fluoride is unstable. Ammonia is added to form diammine silver fluoride $[Ag(NH_3)_2^+]F$. Diammine silver fluoride has a linear structure which is more stable than that of silver fluoride. Like most silver compounds, SDF is unstable under light irradiation and decomposes to silver. Hence, SDF must be stored in a light-proof bottle. It should be used as soon as possible once it is dispensed from the bottle in clinical practice.

Although manufacturers produce SDF according to their own formulation, researchers mostly assume that a 38% SDF solution contains 253,870 ppm silver and 44,800 ppm fluoride ions. In other words, a 38% SDF solution is composed of 25% silver ions and 5% fluoride ions dissolved in an 8% ammonia solution. However, studies have found significant variations in silver and fluoride ion concentration in different SDF products [63–65]. This might be because a 38% SDF solution could be any combination of silver, fluoride and ammonia that totals 38%. Because the concentration of silver, fluoride and ammonia falls within an average range, SDF may not be exactly 38% [66]. In addition, the studies measured the SDF solutions' fluoride concentration via an ion-selective electrode method. This method is non-contaminating and has a short response time. Nevertheless, its precision is not high and the measurement for SDF in the studies could be less robust because of the small samples' dilution.

4. Safety of SDF

Dentists have been using SDF since the 1960s with success for caries arrest. Apart from staining of the carious lesion, literature reported no other significant complications associated with SDF therapy. A clinical trial on 375 young children found that no severe reaction after SDF application. Another clinical study on 126 adults found that no severe erythema after SDF application [39]. SDF can cause transient gingival irritation requiring no treatment [67]. A systematic review concluded that SDF causes mild, reversible pulpal inflammation and is generally biocompatible [68]. A clinical study on six healthy adults found that the fluoride concentrations in serum after SDF application posed little toxicity risk [69]. Another study on 55 children found SDF is safe, and serum concentrations of fluoride pose little risk of toxicity [70]. A study showed that the risk of fluoride toxicity in a young child is low even SDF is applied to all the 20 primary teeth [71].

5. Properties of SDF solution

When silver combines with fluoride in an ammonia solution, silver and fluoride ions are released. Silver is antibacterial. Bacterial resistance against silver is hard to develop because silver kills bacteria through multiple pathways [72]. Silver interferes with bacterial metabolism. It is an oxidising agent that interacts with the sulfhydryl group of proteins and the deoxyribonucleic acid (DNA) of bacteria. The interaction impedes cellular respiratory processes, alters cell wall synthesis, unwinds DNA, and inhibits cell division [73]. Silver also inactivates the bacterial enzyme glycosyltransferase, thus inhibiting biofilm formation. Glycosyltransferases synthesise glucan, which is responsible for bacterial adhesion and the thickening of biofilms on tooth surfaces [74]. Silver also inhibits the proteolytic activities of collagenases to prevent degradation of dentine collagen [62]. In addition, silver reduces bacterial adhesion by incorporating silver into hydroxyapatite to form silver-containing hydroxyapatite in enamel and dentine [75,76].

Fluoride is well known as a remineralisation agent. Fluoride can react with hydroxyapatite to form fluoride-substituted hydroxyapatite via ion exchange of fluoride ions for hydroxyl ions and/or crystal growth of fluorapatite from saliva [62]. Fluoride-substituted hydroxyapatite is more acid-resistant than hydroxyapatite. Hence, enamel or dentine with fluoride-substituted hydroxyapatite is resilient to acid attack. Furthermore, fluoride can precipitate as calcium fluoride. Calcium fluoride is adsorbed and loosely bound onto the tooth surface. Although researchers have various views on this loosely bound calcium fluoride in the oral cavity, many accept that the calcium fluoride can act as a depot and release fluoride ions under an acidic environment to form fluorohydroxyapatite steadily [77]. Fluoride at a high concentration has antimicrobial effects on cariogenic bacteria [78]. Fluoride ions can bind to bacterial enzymes to inhibit the carbohydrate metabolism of acidogenic bacteria as well as their sugar uptake [79,80].

Researchers generally accept that silver and fluoride have a synergistic caries-arresting effect [20,62]. Reviews have concluded that SDF inhibits biofilm formation, promotes remineralisation, counteracts demineralisation, prevents collagen degradation and occludes dentinal tubules [62,81]. These desirable properties of SDF make it an effective agent for management of dental caries and dentine hypersensitivity. Most SDF solutions are alkaline with a pH value of 9–10. The strong alkalinity contributes to the inhibition of the proteolytic activities of collagenases, which can break down dentine collagen. The alkalinity of Riva Star is very high with a pH value of about 13, which can burn the gingiva. To reduce the risk of gingival irritation, the manufacturer produced an ammonia-free silver fluoride solution (Riva Star Aqua). Because Riva Star Aqua is an aqueous silver fluoride solution without the ammonia base, it tastes and smells better than Riva Star.

5.1. SDF inhibits bacterial growth and biofilm formation

SDF inhibits the growth of cariogenic bacteria [79,81]. The minimum inhibitory concentration and minimum bactericidal concentration of SDF for *S. mutans* are lower than that of silver ammonium nitrate and sodium fluoride, showing that SDF is more effective compared to silver ammonium nitrate and sodium fluoride in inhibiting bacterial growth. SDF possesses strong antimicrobial action against *S. mutans*, *A. naeslundii* and *L. acidophilus* [24,82]. *S. mutans* is an important pathogen associated with the initiation and progression of carious lesions. SDF can inhibit the adherence and growth of *S. mutans* on the surface of carious lesions [82]. *L. acidophilus* is often found abundantly in dentine carious lesions [81]. *A. naeslundii* can invade rapidly through dentinal tubules and is attributed to the development of root caries. Studies have shown that SDF inhibited the growth of multispecies cariogenic biofilms containing *S. mutans, A. naeslundii,* and *L. acidophilus* on the tooth surface [79], as well as *E. faecalis* biofilm on root canals [81]. An in vitro study found silver particles, together with dead bacteria on the dentine surface after SDF application [82]. Although SDF is an antibacterial, two *ex vivo* studies found no significant change in the overall microbiome in the arrested carious lesions treated with SDF [38,83]. However, these two studies had a small sample size, and more well-designed clinical studies are required to validate the results.

5.2. SDF promotes remineralisation and counteracts demineralisation

Arrested carious lesions treated with SDF generally have a black and hard surface. This clinical observation is corroborated by an *ex vivo* study that reported an increase in microhardness of the dentine surface layer after SDF application [84]. Laboratory studies found the surface layer of dentine carious lesions was rich in calcium and phosphorus after SDF treatment [29,84]. Saliva is supersaturated with calcium and phosphate. In the presence of saliva, SDF fosters remineralisation of teeth in the oral cavity when the pH value is higher than 5.5 [78]. SDF also inhibits calcium dissolution from hydroxyapatite and prevents the demineralisation of enamel and dentine [85]. A study found that enamel carious lesions, after SDF application, had significantly less mineral loss compared to those without SDF treatment [86]. The plaque on the tooth surfaces absorbs fluoride after SDF application. When bacteria produce acids, the fluoride in the plaque fluid, along with the acids produced, penetrates subsurface of enamel. The fluoride is adsorbed to the crystal surface and protects the crystal from dissolution [87]. In addition, calcium fluoride, silver phosphate and silver protein can be formed and precipitate on the dentine surface after SDF application [88]. A study showed these precipitates developed dense granular structures of spherical grains on the intertubular area of dentine and occluded orifices of dentinal tubules [89]. The precipitates containing high silver and phosphorus content decreased calcium and phosphorous loss from the dentine carious lesions. Although silver phosphate forms in the precipitates, it is relatively unstable, and silver chloride will replace it [24,90]. This is because the solubility product of silver chloride is lower than that of silver phosphate [62].

5.3. SDF inactivates proteolytic activity and prevents collagen degradation

The pathogenesis of enamel caries and dentine caries are not the same. Enamel predominantly consists of the mineral hydroxyapatite (95%) with trace amounts (> 1%) of organic matter by weight percentage. Dentine contains approximately 70% mineral by weight, mainly hydroxyapatite; 20% organic matrix, mainly type I collagen; and 10% fluid. The type I collagen in dentine forms a structural backbone that holds the hydroxyapatite together [81]. In an acidic environment, such as an active carious lesion, or when cariogenic bacteria produce lactic acid, collagenases are activated which destroy dentine collagen. SDF has an inhibitory effect on collagenases, such as matrix metalloproteinases (MMPs) and cysteine cathepsins [25,91]. MMPs are endopeptidases found in the dentine matrix and in saliva. MMPs, in particular MMP-2 (gelatinase A), MMP-8 (neutrophil collagenases) and MMP-9 (gelatinase B), play a crucial role in collagen breakdown in carious lesions. Cysteine cathepsins are proteolytic enzymes found in dentine carious lesions and dental pulp. Cathepsin B can break down collagens, and cathepsin K can catabolise collagen. Activation of MMPs and cysteine cathepsins contributes to collagen breakdown in dentine carious lesions.

Inactivation of collagenases and prevention of collagen degradation contributes to the arrest of carious lesions using SDF [91–93].

5.4. SDF occludes dentinal tubules and promotes tertiary dentine formation

The fluorohydroxyapatite produced after SDF application promotes remineralisation, which can block or decrease tubule diameter, resulting in relief of dentine hypersensitivity [81]. Silver also precipitates as silver salts on the dentine surface and within the dentinal tubules after SDF application [94,95]. Studies have found that the silver deposits can penetrate deep into dentinal tubules [96–98]. The primary mineral precipitates that form after SDF application are calcium phosphates and silver salts [62]. The calcium phosphates can be needle-shaped precipitates that contain calcium, fluoride and phosphorus. The silver salts can be crystals containing silver and chloride [99]. A study found that the precipitated particles became angular and larger, suggesting the presence of secondary crystallisation [98]. Although SDF can penetrate very deep into dentine through patent dentinal tubules, a systematic review concluded that SDF caused no or mild inflammatory response of dental pulp, even though the remaining dentine was thin (0.25–0.50 mm) [100]. A study observed increased cellular activity of the odontoblasts in the dental pulp with the formation of tertiary dentine after SDF application [101]. Thus far, little is known regarding the presence of bacteria within the dentine–pulp complex when SDF is applied to deep carious lesions. A case report found no viable microorganisms within dentine or inside the tooth pulp after SDF application [97].

6. Clinical applications of SDF

Dentists use SDF to desensitise hypersensitive teeth, manage dental caries, remineralise hypomineralised molars, disinfect root canals, manage dental erosion and treat gross gingivitis. They favour SDF therapy because of its ample advantages. First, SDF is effective in arresting caries. Hence, it can be used as non-restorative caries management for controlling pain and infection. Second, is inexpensive. Numerous manufacturers produce SDF at an affordable cost. Third, SDF therapy is straightforward. SDF therapy's simplicity allows dentists, physicians and other qualified health personnel such as hygienists to apply SDF with simple training. Fourth, SDF therapy is painless. Patients generally accept the painless application well, which helps to alleviate patients' fear and anxiety and develop cooperation during treatment. It is particularly useful for treating young children, older adults and people with special needs. Fifth, SDF therapy is non-invasive and non-aerosol-generating. In particular, it can be used to control caries during the COVID-19 pandemic because of its low risk of cross-infection. Finally, SDF requires minimal support and does not require sophisticated or expensive equipment. The simple armamentarium allows clinicians to deliver SDF therapy as an outreach service to people who live in remote areas.

The main disadvantage of SDF therapy is permanent black staining on carious lesions. The staining is primarily to active dental caries. Stains to sound enamel and root dentine are minor and can be polished away. Patients must be well informed before treatment to avoid patient dissatisfaction. SDF also stains the skin, working table, dental instruments and clothes if it is handled carelessly. The stain SDF causes on clothes and dental instruments can be permanent. The stain on the skin often lasts for a few weeks. Although it does not cause any pain, stains on patients' lips, chin or face or the workers' hands are unaesthetic, affecting their social life. Handling with care and using a tinted SDF solution helps prevent this mishap. A scoping review concluded that the staining of arrested carious lesions in children did not influence parental satisfaction [102]. A manufacturer suggests a two-step process using potassium iodide to reduce staining under restorations. The potassium iodide treatment is intended for use when a tooth is being restored, often with a sandwich restoration. When the caries lesion is left exposed to light, there is staining even when potassium iodide is used A clinical trial found the application of potassium iodide in the long term does not reduce the blackening of arrested caries lesions caused by SDF [103]. Dentists can use glass ionomer cement or composite resin restoration to restore the SDF-treated lesion at another appointment. In this case, the SDF serves to obviate the need for local anaesthetic.

SDF also has an unpleasant metallic taste. Some clinicians apply fluoride varnish on the top of the SDF to mask the unpleasant taste of SDF [104,105]. The varnish can also be a protective layer to prolong contact of the SDF with the tooth surface. Proper isolation of the tooth can avoid SDF contacting the tongue and enhance the patient's acceptance of SDF therapy. Furthermore, SDF may induce transient gingival and mucosal irritation. In general, the irritation will spontaneously heal and require no treatment. Direct application of SDF to dental pulp causes pulp necrosis [100]. However, indirect SDF application generally does not cause a significant inflammatory response of dental pulp [101]. A 30-month clinical trial on young children found SDF therapy did not cause acute systemic side effects [106]. In addition, toothache or gum pain, gum swelling and gum bleaching after SDF application were uncommon. In general, studies in Hong Kong and the United States reported that parents generally accepted SDF therapy for their children [107–109].

6.1. Treating dentine hypersensitivity

Dentine hypersensitivity arises from exposed dentine surfaces in response to stimuli such as cold and touch. Dentine hypersensitivity can result in severe, persistent pain and discomfort [110]. Laboratory studies have found evidence of occlusion of dentinal tubules of dentine after SDF application [94,98,111]. Clinical studies showed topical application of SDF relieved pain in adults with hypersensitive permanent teeth within one week [39,112–113]. A 38% SDF gel was developed to offer clinicians better control of the application area on the hypersensitive tooth [98]. Some dentists apply SDF on a vital tooth in preparation for extra-coronal restoration to reduce postoperative sensitivity. Glass ionomer and resin-modified glass ionomer can be used as luting cements because SDF does not affect their bond strength [26,114]. A study reported that SDF adversely affected the bond strength between dentine and some resin adhesives [115].

6.2. Managing dental caries

SDF is an archetypal example of non-restorative caries treatment that steers sustainable caries management through controlling bacterial infection and remineralising teeth. Dentists use SDF to arrest early childhood caries. A systematic review reported that the overall rate of caries arrest was 81% in primary teeth [2]. Some researchers proposed using SDF for caries prevention [116]. However, an umbrella review concluded there was insufficient evidence to draw conclusions on SDF for prevention in primary teeth and prevention and arrest in permanent teeth in children [117]. More well-designed clinical trials are needed to evaluate SDF's effectiveness in preventing caries development. SDF is also used to manage root caries. Root caries are very challenging to restore due to the proximity to the pulp and the location of the carious lesion [103]. Current evidence shows SDF therapy is an effective fluoride agent for arresting root caries [118–121]. Annual SDF application is a simple, inexpensive and effective way of preventing the initiation and progression of root caries in older adults [118]. A systematic review found the preventive fraction of SDF for preventing root caries ranged from 50% to 68% [119]. Two reviews found that annual application of 38% SDF was the most effective treatment among the different treatments for preventing root caries [120,121].

6.3. Remineralising hypomineralised molars

Hypomineralisation of teeth is a developmental defect that usually affects permanent incisors and first molars [122]. Well-demarcated opacities, which can be chalky white to dark brown in colour, characterise clinically hypomineralised teeth [123]. Histologically, the opacities are porous and located in the inner part of the enamel. Children with hypomineralised teeth often suffer from severe hypersensitivity due to rapid tooth wear and exposure of dentine. They also have a high risk of caries because of defective enamel in the hypomineralised teeth. SDF is a simple, painless and non-invasive therapy for managing hypomineralised teeth. SDF application effectively desensitises a hypomineralised tooth and quickly arrests carious lesions on it. A clinical study found biannual SDF application prevented caries development and reduced dentine hypersensitivity in hypomineralised molars [123]. The study concluded that SDF application continued through repeated applications on hypomineralised teeth provides profound and long-lasting relief of dentine hypersensitivity.

6.4. Disinfecting a root canal in endodontic therapy

Chronic periapical periodontitis is a common endodontic infection that causes failure of endodontic treatment. SDF is available at a low concentration of 3.8% for managing endodontic infection. The infection is often associated with *E. faecalis* [124]. Studies found irrigation with a 3.8% SDF solution in endodontic treatment was effective in removing *E. faecalis* biofilms in root canals [125,126]. SDF disinfects and prevents reinfection of the root canals. SDF can absorb and kill dentinophilic bacteria in the circumpulpal dentine [126,127]. The silver salts of SDF precipitate and obliterate the dentinal tubules and prevent bacteria from reinfecting the disinfected dentinal tubules. Researchers suggested the silver salts may provide a potential means of substantivity that permits the gradual release of silver ions over time. Furthermore, researchers reported that SDF decreased the permeability, increased the surface hardness and strengthened the fracture resistance of the root canal [6, 12, 128]. However, clinical studies verifying the results of the laboratory studies are lacking.

6.5. Managing dental erosion

Dental erosion is an acid dissolution of tooth structure that does not involve bacteria [129]. The loss of tooth structure with open dentinal tubules often initiates dentine hypersensitivity, which can result in severe, persistent pain and discomfort. SDF is an effective anti-erosive agent with remineralising properties [84]. It reacts with the teeth's minerals to form metallic silver and silver chloride on tooth surfaces [24,25]. A study found silver-containing hydroxyapatite on enamel after SDF application [27]. These silver composites' formation plausibly enables SDF to prevent dental erosion. A laboratory study found SDF was effective in reducing dental erosion in enamel and dentine [10]. SDF can be used for preventing dental erosion once its efficacy is confirmed in clinical studies.

6.6. Treating gross gingivitis

A laboratory study reported that SDF demonstrated significant antibacterial properties against putative periodontal pathogens causing severe periodontitis [130]. The authors suggested that SDF could be a potential new therapeutic agent for management of periodontal infections because SDF suppressed periodontal pathogens in subgingival biofilms. A clinical study reported that SDF can be used to treat hyperplastic gingivitis [131]. The authors found SDF could effectively reduce marginal gingival and papillary inflammation. Another one-year clinical trial found that SDF improved the gingival health of older adults with gingivitis with no adverse effects [132].

7. SDF therapy in outreach service

Conventional dental treatment for dental caries is not accessible, available or affordable in many communities. Using SDF in outreach service can be a pragmatic strategy for caries management [133]. SDF therapy is simple, non-invasive and inexpensive and does not require a sophisticated armamentarium. It is particularly useful for dental outreach services to prevent and arrest caries. Hong Kong and Mongolia are offering region-wide large-scale dental outreach services using SDF to control early childhood caries in preschool-age children. Apart from young children, SDF therapy is a promising strategy for managing dental caries in older adults and those who have special needs when physical limitations do not allow conventional dental treatment. In addition, SDF is non-aerosol-generating and has low risk of cross-infection. It can be used for caries control during the COVID-19 pandemic.

8. Conclusion

In conclusion, SDF is a caries-arresting fluoride agent with antibacterial and mineralising properties. It can inhibit biofilm formation, promote remineralisation, counteract demineralisation, prevent collagen degradation and occlude dentinal tubules. It can be used to arrest early childhood caries, manage root caries, prevent fissure caries, impede secondary caries, desensitise hypersensitive teeth and manage infected root canals. SDF therapy to arrest caries is simple, painless, non-invasive, non-aerosol-generating and inexpensive. Both clinicians and patients generally accept SDF therapy well.

Funding

This research was funded by General Research Fund of the Hong Kong Research Grant Council, grant number 17100019.

Conflict of interest

The authors declare that they have no conflict of interest.

References

[1] Gao SS, Amarquaye G, Arrow P, Bansal K, Bedi R, Campus G, et al. Global oral health policies and guidelines: using silver diamine fluoride for caries control. Front Oral Health 2021;2:685557.

[2] Gao SS, Zhao IS, Hiraishi N, Duangthip D, Mei ML, Lo ECM, Chu CH. Clinical trials of silver diamine fluoride in arresting caries among children: a systematic review. JDR Clin Trans Res 2016;1(3):201–10.

[3] Yamaga R. Arrestment of caries of deciduous teeth with diamine silver fluoride. Dent Outlook 1969;33:1007–13.

[4] Nishino M, Yoshida S. The cariostatic effect and pulp reaction of topically applied ammonical silver fluoride on in primary teeth. Jpn J Pedodont 1969;7:55–9.

[5] Nishino M, Ono S, Kita Y, Tsuchitani Y. Caries prevention in pits and fissures with diammine silver fluoride solution and fissure sealant. Sealing properties of pits and fissures and adhesive characteristics to enamel. J Osaka Univ Dent Sch 1974;14:1–7.

[6] Yamaga R, Nishino M, Yoshida S, Yokomizo I. Diammine silver fluoride and its clinical application. J Osaka Univ Dent Sch 1972;12:1–20.

[7] Ballikaya E, Ünverdi GE, Cehreli ZC. Management of initial carious lesions of hypomineralized molars (MIH) with silver diamine fluoride or silver-modified atraumatic restorative treatment (SMART): 1-year results of a prospective, randomized clinical trial. Clin Oral Investig 2022;26(2):2197–205.

[8] Yamashita H. [Penetration of Ag (NH3)2F applied to an infected root canal]. Gifu Shika Gakkai Zasshi 1985;12(3):417–39. (Japanese).
[9] Liu Y, Zhai W, Du F. [Clinical observation of treatment of tooth hypersensitiveness with silver ammonia fluoride and potassium nitrate solution]. Zhonghua Kou Qiang Yi Xue Za Zhi 1995;30(6):352–4. (Chinese).
[10] Ainoosah SE, Levon J, Eckert GJ, Hara AT, Lippert F. Effect of silver diamine fluoride on the prevention of erosive tooth wear in vitro. J Dent 2020;103S:100015.
[11] Sayed M, Nikaido T, Abdou A, Burrow MF, Tagami J. Potential use of silver diammine fluoride in detection of carious dentin. Dent Mater J 2021;40(3):820–6.
[12] Yokoyama K, Kimura Y, Matsumoto K, Fujishima A, Miyazaki T. Preventive effect of tooth fracture by pulsed Nd:YAG laser irradiation with diamine silver fluoride solution. J Clin Laser Med Surg 2001;19(6):315–8.
[13] Zhang C, Kimura Y, Matsumoto K. The effects of pulsed Nd:YAG laser irradiation with fluoride on root surface. J Clin Laser Med Surg 1996;14(6):399–403.
[14] Mei ML, Ito L, Zhang CF, Lo EC, Chu CH. Effect of laser irradiation on the fluoride uptake of silver diamine fluoride treated dentine. Lasers Med Sci 2015;30(3):985–91.
[15] Rosenblatt A, Stamford TC, Niederman R. Silver diamine fluoride: a caries "silver-fluoride bullet". J Dent Res 2009;88(2):116–25.
[16] World Health Organization Model List of Essential Medicines – 22nd List, 2021. Geneva: World Health Organization; 2021 (WHO/MHP/HPS/EML/2021.02). Licence: CC BY-NC-SA 3.0 IGO.
[17] Crystal YO, Janal MN, Yim S, Nelson T. Teaching and utilization of silver diamine fluoride and Hall-style crowns in US pediatric dentistry residency programs. J Am Dent Assoc 2020;151(10):755–63.
[18] Jiang CM, Duangthip D, Chan AKY, Tamrakar M, Lo ECM, Chu CH. Global research interest regarding silver diamine fluoride in dentistry: a bibliometric analysis. J Dent 2021;113:103778.
[19] Nishino M. [Studies on the topical application of ammoniacal silver fluoride for the arrest of dental caries]. Osaka Daigaku Shigaku Zasshi 1969;14(1):1–14. (Japanese).
[20] Li YJ. [Effect of a silver ammonia fluoride solution on the prevention and inhibition of caries]. Zhonghua Kou Qiang Ke Za Zhi 1984;19(2):97–100. (Chinese).
[21] Duperon DF. Early childhood caries: a continuing dilemma. J Calif Dent Assoc 1995;23(2):15–6.
[22] Almeida I.C.S. Evaluation of the Cariostatic, Anticariogenic and Antimicrobial Effect of 12 Percent Silver Diamine Fluoride Solution (BIORIDE) in Children from 5 1/2 to 6 Years Old. Bauru (Brazil): University of Sao Paulo, 1994. (Master's thesis).
[23] Chu CH, Lo EC, Lin HC. Effectiveness of silver diamine fluoride and sodium fluoride varnish in arresting dentin caries in Chinese pre-school children. J Dent Res 2002;81(11):767–70.
[24] Mei ML, Chu CH, Low KH, Che CM, Lo EC. Caries arresting effect of silver diamine fluoride on dentine carious lesion with S. mutans and L. acidophilus dual-species cariogenic biofilm. Med Oral Patol Oral Cir Bucal 2013;18(6):e824–31.
[25] Mei ML, Ito L, Cao Y, Li QL, Chu CH, Lo EC. The inhibitory effects of silver diamine fluorides on cysteine cathepsins. J Dent 2014;42(3):329–35.
[26] Zhao IS, Chu S, Yu OY, Mei ML, Chu CH, Lo ECM. Effect of silver diamine fluoride and potassium iodide on shear bond strength of glass ionomer cements to caries-affected dentine. Int Dent J 2019;69(5):341–7.
[27] Yu OY, Mei ML, Zhao IS, Li QL, Lo EC, Chu CH. Remineralisation of enamel with silver diamine fluoride and sodium fluoride. Dent Mater 2018;34(12):e344–52.
[28] Mei ML, Ito L, Chu CH, Lo EC, Zhang CF. Prevention of dentine caries using silver diamine fluoride application followed by Er:YAG laser irradiation: an in vitro study. Lasers Med Sci 2014;29(6):1785–91.
[29] Mei ML, Ito L, Cao Y, Lo EC, Li QL, Chu CH. An ex vivo study of arrested primary teeth caries with silver diamine fluoride therapy. J Dent 2014;42(4):395–402.
[30] Tan HP, Lo EC, Dyson JE, Luo Y, Corbet EF. A randomized trial on root caries prevention in elders. J Dent Res 2010;89(10):1086–90.
[31] Zhang W, McGrath C, Lo EC, Li JY. Silver diamine fluoride and education to prevent and arrest root caries among community-dwelling elders. Caries Res 2013;47(4):284–90.
[32] Zhi QH, Lo EC, Lin HC. Randomized clinical trial on effectiveness of silver diamine fluoride and glass ionomer in arresting dentine caries in preschool children. J Dent 2012;40(11):962–7.
[33] Fung MHT, Duangthip D, Wong MCM, Lo ECM, Chu CH. Arresting dentine caries with different concentration and periodicity of silver diamine fluoride. JDR Clin Trans Res 2016;1(2):143–52.
[34] Fung MHT, Duangthip D, Wong MCM, Lo ECM, Chu CH. Randomized clinical trial of 12% and 38% silver diamine fluoride treatment. J Dent Res 2018;97(2):171–8.
[35] Duangthip D, Chu CH, Lo EC. A randomized clinical trial on arresting dentine caries in preschool children by topical fluorides–18 month results. J Dent 2016;44:57–63.
[36] Craig GG, Powell KR, Cooper MH. Caries progression in primary molars: 24-month results from a minimal treatment programme. Community Dent Oral Epidemiol 1981;9(6):260–5.
[37] Knight GM, McIntyre JM, Craig GG, Mulyani, Zilm PS, Gully NJ. An in vitro model to measure the effect of a silver fluoride and potassium iodide treatment on the permeability of demineralized dentine to Streptococcus mutans. Aust Dent J 2005;50(4):242–5.
[38] Milgrom P, Horst JA, Ludwig S, Rothen M, Chaffee BW, Lyalina S, Pollard KS, DeRisi JL, Mancl L. Topical silver diamine fluoride for dental caries arrest in preschool children: a randomized controlled trial and microbiological analysis of caries associated microbes and resistance gene expression. J Dent 2018;68:72–8.
[39] Castillo JL, Rivera S, Aparicio T, Lazo R, Aw TC, Mancl LL, Milgrom P. The short-term effects of diammine silver fluoride on tooth sensitivity: a randomized controlled trial. J Dent Res 2011;90(2):203–8.
[40] Kyoon-Achan G, Schroth RJ, DeMaré D, Sturym M, Edwards J, Lavoie JG, Sanguins J, Campbell R, Chartrand F, Bertone MF, Singh S, Moffatt MEK. Scaling-up Healthy Smile Happy Child team. Indigenous community members' views on silver diamine fluoride to manage early childhood caries. J Public Health Dent 2020;80(3):208–16.
[41] Robertson L.D. Early Childhood Caries in American Indian Children: Looking Beyond the Usual Causes. Ottawa, ON: Canadian Dental Association; (2018). Available online from: 〈http://oasisdiscussions.ca/2018/02/20/ecc-6/〉. (accessed Jul 5, 2022).
[42] Turton B, Patel J, Hill R, Sieng C, Durward C. Healthy Kids Cambodia - A novel approach to triage for dental care in a population with extreme caries experience. Community Dent Oral Epidemiol 2020;48(1):56–62.
[43] Turton B, Patel J, Sieng C, Tak R, Durward C. School based tooth brushing and annual silver diamine fluoride application as a highest priority package for achieving universal oral health care for cambodian children. Front Oral Health 2021;2:667867.
[44] American Dental Association. Silver Diamine Fluoride (2021). Available online from: 〈https://www.ada.org/resources/research/science-and-research-institute/oral-health-topics/silver-diamine-fluoride〉. (accessed Jul 5, 2022).
[45] Gao SS, Zhao IS, Duffin S, Duangthip D, Lo ECM, Chu CH. Revitalising silver nitrate for caries management. Int J Environ Res Public Health 2018;15(1):80.
[46] Momoi Y, Hayashi M, Fujitani M, Fukushima M, Imazato S, Kubo S, Nikaido T, Shimizu A, Unemori M, Yamaki C. Clinical guidelines for treating caries in adults following a minimal intervention policy–evidence and consensus based report. J Dent 2012;40(2):95–105.
[47] Sitthisettapong T, Tasanarong P, Phantumvanit P. Strategic management of early childhood caries in thailand: a critical overview. Front Public Health 2021;9:664541.
[48] Current Care Guidelines (Käypähoito suositus). Caries Management Guidelines 2020. (2020). Available online from: 〈https://www.kaypahoito.fi/en/about-current-care guidelines〉 (accessed Jul 5, 2022).
[49] Paris S, Banerjee A, Bottenberg P, Breschi L, Campus G, Doméjean S, et al. How to intervene in the caries process in older adults: a Joint ORCA and EFCD Expert Delphi Consensus Statement. Caries Res 2020;54:1–7.
[50] Splieth CH, Banerjee A, Bottenberg P, Breschi L, Campus G, Ekstrand KR, et al. How to intervene in the caries process in children: a Joint ORCA and EFCD Expert Delphi Consensus Statement. Caries Res 2020;1:1–9.
[51] Subbiah GK, Gopinathan NM. Is silver diamine fluoride effective in preventing and arresting caries in elderly adults? A systematic review. J Int Soc Prev Community Dent 2018;8:191–9.
[52] Toumba KJ, Twetman S, Splieth C, Parnell C, van Loveren C, Lygidakis N. Guidelines on the use of fluoride for caries prevention in children: an updated EAPD policy document. Eur Arch Paediatr Dent 2019;20:507–16.
[53] Office of the Chief Dental Officer. Standard Operating Procedure. Transition to Recovery. (2020). Available online from: 〈https://www.dentistry.co.uk/wpcontent/uploads/2020/06/C0575-dental-transition-to-recovery-sop-4-June.pdf〉 (accessed Jul 5, 2022).
[54] British Society of Paediatric Dentistry. (2020). Available online from: 〈https://www.bspd.co.uk/Professionals/Resourcs〉 (accessed Jul 5, 2022).
[55] Lamberghini F. Silver diamine fluoride: a new way to treat caries in Canada. CDA Essentials [Internet]. 2017;4(3):21–2. Available online from: 〈https://www.cda-adc.ca/en/services/essentials/2017/issue8/17/〉.(accessed Jul 5, 2022).
[56] Crystal YO, Marghalani AA, Ureles SD, Wright JT, Sulyanto R, Divaris K, et al. Use of silver diamine fluoride for dental caries management in children and adolescents, including those with special health care needs. Pediatr Dent 2017;39:135E–145EE.
[57] Slayton RL, Urquhart O, Araujo MWB, Fontana M, Guzmán-Armstrong S, Nascimento MM, et al. Evidence-based clinical practice guideline on nonrestorative treatments for carious lesions: a report from the American Dental Association. J Am Dent Assoc 2018;149(10):837–49.
[58] Brasil. Ministério da Saúde. Secretaria de Atenção Primária à Saúde. Departamento de Saúde da Família. Carteira de serviços da Atenção Primária à Saúde (CaSAPS): versão profissionais de saúde e gestores. Brasília: Ministério da Saúde. (2020). Available online from:〈http://189.28.128.100/dab/docs/portaldab/documentos/casaps_versao_profissionais_saude_gestores_completa.pdf〉.(accessed Jul 5, 2022).
[59] Associação Brasileira de Odontopediatria. Diamino Fluoreto de Prata. In: Associação Brasileira de Odontopediatria, editor. Diretrizes para procedimentos clínicos em Odontopediatria. Rio de Janeiro: Santos 2020. 114–118.
[60] Do L. Guidelines for use of fluorides in Australia: update 2019. Aust Dent J 2020;65:30–8.
[61] Yee R, Holmgren C, Mulder J, Lama D, Walker D, van Palenstein Helderman W. Efficacy of silver diamine fluoride for Arresting Caries Treatment. J Dent Res 2009;88(7):644–7.
[62] Mei ML, Lo ECM, Chu CH. Arresting dentine caries with silver diamine fluoride: what's behind it? J Dent Res 2018;97(7):751–8.
[63] Patel J, Foster D, Smirk M, Turton B, Anthonappa R. Acidity, fluoride and silver ion concentrations in silver diamine fluoride solutions: a pilot study. Aust Dent J 2021;66(2):188–93.

[64] Crystal YO, Rabieh S, Janal MN, Rasamimari S, Bromage TG. Silver and fluoride content and short-term stability of 38% silver diamine fluoride. J Am Dent Assoc 2019;150(2):140–6.
[65] Mei ML, Chu CH, Lo EC, Samaranayake LP. Fluoride and silver concentrations of silver diammine fluoride solutions for dental use. Int J Paediatr Dent 2013;23(4):279–85.
[66] Milgrom P. Omissions make silver diamine fluoride paper impossible to interpret. Aust Dent J 2021;66(2):212–3.
[67] Llodra JC, Rodriguez A, Ferrer B, Menardia V, Ramos T, Morato M. Efficacy of silver diamine fluoride for caries reduction in primary teeth and first permanent molars of schoolchildren: 36-month clinical trial. J Dent Res 2005;84(8):721–4.
[68] Zaeneldin A, Yu OY, Chu CH. Effect of silver diamine fluoride on vital dental pulp: a systematic review. J Dent 2022;119:104066.
[69] Vasquez E, Zegarra G, Chirinos E, Castillo JL, Taves DR, Watson GE, Dills R, Mancl LL, Milgrom P. Short term serum pharmacokinetics of diammine silver fluoride after oral application. BMC Oral Health 2012;12:60.
[70] Ellenikiotis H, Chen KF, Soleimani-Meigooni DN, Rothen ML, Thompson B, Lin YS, Milgrom P. Pharmacokinetics of 38 percent silver diamine fluoride in children. Pediatr Dent 2022;44(2):114–21.
[71] Yan IG, Zheng FM, Gao SS, Duangthip D, Lo ECM, Chu CH. Fluoride delivered via a topical application of 38% SDF and 5% NaF. Int Dent J 2022;S0020–6539(22):00066-1.
[72] Wu MY, Suryanarayanan K, van Ooij WJ, Oerther DB. Using microbial genomics to evaluate the effectiveness of silver to prevent biofilm formation. Water Sci Technol 2007;55(8–9):413–9.
[73] Oppermann RV, Johansen JR. Effect of fluoride and non-fluoride salts of copper, silver and tin on the acidogenicity of dental plaque in vivo. Scand J Dent Res 1980;88(6):476–80.
[74] Tamesada M, Kawabata S, Fujiwara T, Hamada S. Synergistic effects of streptococcal glucosyltransferases on adhesive biofilm formation. J Dent Res 2004;83(11):874–9.
[75] Chen W, Liu Y, Courtney HS, Bettenga M, Agrawal CM, Bumgardner JD, Ong JL. In vitro anti-bacterial and biological properties of magnetron co-sputtered silver-containing hydroxyapatite coating. Biomaterials 2006;27(32):5512–7.
[76] Singh B, Dubey AK, Kumar S, Saha N, Basu B, Gupta R. In vitro biocompatibility and antimicrobial activity of wet chemically prepared Ca10− xAgx (PO4) 6 (OH) 2 (0.0≤ x≤ 0.5) hydroxyapatites. Mater Sci Eng C 2011;31(7):1320–9.
[77] Ten Cate JM. Contemporary perspective on the use of fluoride products in caries prevention. Br Dent J 2013;214(4):161–7.
[78] Buzalaf MAR, Pessan JP, Honório HM, Ten, Cate JM. Mechanisms of action of fluoride for caries control. Monogr Oral Sci 2011;22:97–114.
[79] Mei ML, Li QL, Chu CH, Lo EC, Samaranayake LP. Antibacterial effects of silver diamine fluoride on multi-species cariogenic biofilm on caries. Ann Clin Microbiol Antimicrob 2013;12:4.
[80] Koo H. Strategies to enhance the biological effects of fluoride on dental biofilms. Adv Dent Res 2008;20(1):17–21.
[81] Zhao IS, Gao SS, Hiraishi N, Burrow MF, Duangthip D, Mei ML, Lo EC, Chu CH. Mechanisms of silver diamine fluoride on arresting caries: a literature review. Int Dent J 2018;68(2):67–76.
[82] Chu CH, Mei L, Seneviratne CJ, Lo EC. Effects of silver diamine fluoride on dentine carious lesions induced by Streptococcus mutans and Actinomyces naeslundii biofilms. Int J Paediatr Dent 2012;22(1):2–10.
[83] Mei ML, Yan Z, Duangthip D, Niu JY, Yu OY, You M, Lo ECM, Chu CH. Effect of silver diamine fluoride on plaque microbiome in children. J Dent 2020;102:103479.
[84] Chu CH, Lo EC. Microhardness of dentine in primary teeth after topical fluoride applications. J Dent 2008;36(6):387–91.
[85] Wu L, Yang F. Comparison of the effects of three fluoride-containing agents on the demineralization of deciduous teeth in vitro. J Mod Stomatol 2002;16:216–8.
[86] Rosas SGP, Téllez MÁA, Espinoza EV. In vitro efficiency of fluoride-containing compounds on remineralization of carious enamel lesions under cyclic pH conditions. Rev Odontol Mex 2014;18(2):96–104.
[87] Featherstone JD. Prevention and reversal of dental caries: role of low level fluoride. Community Dent Oral Epidemiol 1999;27(1):31–40.
[88] Yu DG, Kimura Y, Fujita A, Hossain M, Kinoshita JI, Suzuki N, Matsumoto K. Study on acid resistance of human dental enamel and dentin irradiated by semiconductor laser with Ag(NH3)2F solution. J Clin Laser Med Surg 2001;19(3):141–6.
[89] Mei ML, Ito L, Cao Y, Li QL, Lo EC, Chu CH. Inhibitory effect of silver diamine fluoride on dentine demineralisation and collagen degradation. J Dent 2013;41(9):809–17.
[90] Mei ML, Nudelman F, Marzec B, Walker JM, Lo ECM, Walls AW, Chu CH. Formation of fluorohydroxyapatite with silver diamine fluoride. J Dent Res 2017;96(10):1122–8.
[91] Mei ML, Li QL, Chu CH, Yiu CK, Lo EC. The inhibitory effects of silver diamine fluoride at different concentrations on matrix metalloproteinases. Dent Mater 2012;28(8):903–8.
[92] Chaussain-Miller C, Fioretti F, Goldberg M, Menashi S. The role of matrix metalloproteinases (MMPs) in human caries. J Dent Res 2006;85(1):22–32.
[93] Altinci P, Mutluay M, Seseogullari-Dirihan R, Pashley D, Tjäderhane L, Tezvergil-Mutluay A. NaF inhibits matrix-bound cathepsin-mediated dentin matrix degradation. Caries Res 2016;50(2):124–32.
[94] Li Y, Liu Y, Psoter WJ, Nguyen OM, Bromage TG, Walters MA, et al. Assessment of the silver penetration and distribution in carious lesions of deciduous teeth treated with silver diamine fluoride. Caries Res 2019;53(4):431–40.
[95] Pashley DH. Mechanisms of dentin sensitivity. Dent Clin N Am 1990;34(3):449–73.
[96] Rossi G, Squassi A, Mandalunis P, Kaplan A. Effect of silver diamine fluoride (SDF) on the dentin-pulp complex: ex vivo histological analysis on human primary teeth and rat molars. Acta Odontol Lat 2017;30(1):5–12.
[97] Bimstein E, Damm D. Human primary tooth histology six months after treatment with silver diamine fluoride. J Clin Pediatr Dent 2018;42(6):442–4.
[98] Kiesow A, Menzel M, Lippert F, Tanzer JM, Milgrom P. Dentin tubule occlusion by a 38% silver diamine fluoride gel: an in vitro investigation. BDJ Open 2022;8(1):1.
[99] Peng JJ, Botelho MG, Matinlinna JP. Silver compounds used in dentistry for caries management: a review. J Dent 2012;40(7):531–41.
[100] Zaeneldin A, Yu OY, Chu CH. Effect of silver diamine fluoride on vital dental pulp: a systematic review. J Dent 2022;119:104066.
[101] Korwar A, Sharma S, Logani A, Shah N. Pulp response to high fluoride releasing glass ionomer, silver diamine fluoride, and calcium hydroxide used for indirect pulp treatment: an in-vivo comparative study. Conte Clin Dent 2015;6(3):288–92.
[102] Magno MB, Silva LPD, Ferreira DM, Barja-Fidalgo F, Fonseca-Gonçalves A. Aesthetic perception, acceptability and satisfaction in the treatment of caries lesions with silver diamine fluoride: a scoping review. Int J Paediatr Dent 2019;29(3):257–66.
[103] Li R, Lo EC, Liu BY, Wong MC, Chu CH. Randomized clinical trial on arresting dental root caries through silver diammine fluoride applications in community-dwelling elders. J Dent 2016;51:15–20.
[104] Mitchell C, Gross AJ, Milgrom P, Mancl L, Prince DB. Silver diamine fluoride treatment of active root caries lesions in older adults: a case series. J Dent 2021;105:103561.
[105] Sihra R, Schroth RJ, Bertone M, Martin H, Patterson B, Mittermuller BA, et al. The effectiveness of silver diamine fluoride and fluoride varnish in arresting caries in young children and associated oral health-related quality of life. J Can Dent Assoc 2020;86.
[106] Duangthip D, Fung MHT, Wong MCM, Chu CH, Lo ECM. Adverse effects of silver diamine fluoride treatment among preschool children. J Dent Res 2018;97(4):395–401.
[107] Huebner CE, Milgrom P, Cunha-Cruz J, Scott J, Spiekerman C, Ludwig S, et al. Parents' satisfaction with silver diamine fluoride treatment of carious lesions in children. J Dent Child 2020;87(1):4–11.
[108] Crystal YO, Janal MN, Hamilton DS, Niederman R. Parental perceptions and acceptance of silver diamine fluoride staining. J Am Dent Assoc 2017;148(7):510–8.
[109] Duangthip D, Fung MHT, Wong MCM, Chu CH, Lo ECM. Adverse effects of silver diamine fluoride treatment among preschool children. J Dent Res 2018;97(4):395–401.
[110] Chu CH, Lam A, Lo EC. Dentin hypersensitivity and its management. Gen Dent 2011;59(2):115–22.
[111] Peng JY, Botelho MG, Matinlinna JP, Pan HB, Kukk E, Low KJ. Interaction of storage medium and silver diamine fluoride on demineralized dentin. J Int Med Res 2021;49(2). 300060520985336.
[112] Ma RL. [Clinical observation of treatment of tooth hypersensitivity with silver ammonia fluoride solution]. Zhonghua Kou Qiang Yi Xue Za Zhi 1993;28(1):30–1. (Chinese).
[113] Craig GG, Knight GM, McIntyre JM. Clinical evaluation of diamine silver fluoride/potassium iodide as a dentine desensitizing agent. A pilot study. Aust Dent J 2012;57(3):308–11.
[114] Al-Qahtani YM. Impact of graphene oxide and silver diamine fluoride in comparison to photodynamic therapy on bond integrity and microleakage scores of resin modified glass ionomer cement to demineralized dentin. Photodiag Photodyn Ther 2021;33:102163.
[115] Braz PVF, Dos Santos AF, Pereira PN, Ribeiro APD. Silver diamine fluoride and cleaning methods effects on dentin bond strength. Am J Dent 2020;33(6):315–9.
[116] Contreras V, Toro MJ, Elías-Boneta AR, Encarnación-Burgos A. Effectiveness of silver diamine fluoride in caries prevention and arrest: a systematic literature review. Gen Dent 2017;65(3):22–9.
[117] Seifo N, Cassie H, Radford JR, Innes NPT. Silver diamine fluoride for managing carious lesions: an umbrella review. BMC Oral Health 2019;19(1):145.
[118] Oliveira BH, Cunha-Cruz J, Rajendra A, Niederman R. Controlling caries in exposed root surfaces with silver diamine fluoride: a systematic review with meta-analysis. J Am Dent Assoc 2018;149(8):671–9.
[119] Gold J. Silver diamine fluoride may prevent and arrest root caries in older adults. J Evid Based Dent Pract 2019;19(2):186–8.
[120] Castelo R, Attik N, Catirse ABCEB, Pradelle-Plasse N, Tirapelli C, Grosgogeat B. Is there a preferable management for root caries in middle-aged and older adults? A systematic review. Br Dent J 2021.
[121] Zhang J, Sardana D, Li KY, Leung KCM, Lo ECM. Topical fluoride to prevent root caries: systematic review with network meta-analysis. J Dent Res 2020;99(5):506–13.
[122] Weerheijm KL. Molar incisor hypomineralisation (MIH). Eur J Paediatr Dent 2003;4(3):114–20.
[123] Da Costa-Silva CM, Ambrosano GM, Jeremias F, De Souza JF, Mialhe FL. Increase in severity of molar-incisor hypomineralization and its relationship with the

colour of enamel opacity: a prospective cohort study. Int J Paediatr Dent 2011;21(5):333–41.
[124] Wang QQ, Zhang CF, Chu CH, Zhu XF. Prevalence of Enterococcus faecalis in saliva and filled root canals of teeth associated with apical periodontitis. Int J Oral Sci 2012;4(1):19–23.
[125] Al-Madi EM, Al-Jamie MA, Al-Owaid NM, Almohaimede AA, Al-Owid AM. Antibacterial efficacy of silver diamine fluoride as a root canal irrigant. Clin Exp Dent Res 2019;5(5):551–6.
[126] Hiraishi N, Yiu CK, King NM, Tagami J, Tay FR. Antimicrobial efficacy of 3.8% silver diamine fluoride and its effect on root dentin. J Endod 2010;36(6):1026–9.
[127] Knight GM, McIntyre JM, Craig GG, Mulyani, Zilm PS, Gully NJ. Inability to form a biofilm of Streptococcus mutans on silver fluoride- and potassium iodide-treated demineralized dentin. Quintessence Int 2009;40(2):155–61.
[128] Yokoyama K, Matsumoto K, Murase J. Permeability of the root canal wall and occlusion of dentinal tubules by Ag(NH3)2F: a comparison of combined use with pulsed Nd:YAG laser or iontophoresis. J Clin Laser Med Surg 2000;18(1):9–14.
[129] da Cunha WA, Palma LF, Shitsuka C, Corrêa FNP, Duarte DA, Corrêa MSNP. Efficacy of silver diamine fluoride and sodium fluoride in inhibiting enamel erosion: an ex vivo study with primary teeth. Eur Arch Paediatr Dent 2021;22(3):387–92.
[130] Rams TE, Sautter JD, Ramírez-Martínez GJ, Whitaker EJ. Antimicrobial activity of silver diamine fluoride on human periodontitis microbiota. Gen Dent 2020;68(5):24–8.
[131] Lim GXD, Yang J. Effect of silver diamine fluoride on hyperplastic gingivitis in an adult with intellectual disability-A case report. Spec Care Dent 2022;42(1):73–9.
[132] Alshehri W. Effect of Silver diamine fluoride on the treatment of gingivitis in geriatric patients. Texas A&M University; 2020. (Doctoral dissertation).
[133] Chen KJ, Gao SS, Duangthip D, Lo ECM, Chu CH. Managing early childhood caries for young children in China. Healthcare 2018;6(1):11.