Contemporary Pediatric Dentistry

Review
Contemp Pediatr Dent 2021:2(1):1-13
DOI: 10.51463/cpd.2021.47

Nanosilver fluoride as a caries arresting agent: A narrative review

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Highlights

The current paper foregrounds the effectiveness of a non-invasive treatment approach for dental caries using caries arresting agents.

The newer nanotechnology-based caries arresting agent presents effective antibacterial properties against cariogenic bacteria and modulation of the demineralization-remineralization balance for teeth.

The silver nanoparticle-based preparations present to overcome the limitations of using silver ion-based solutions for caries arrest.

Abstract

Dental caries is the most prevalent oral disease that continues to affect almost every country in the world. The contemporary management of dental caries focuses on non-restorative, non-invasive, and micro-invasive treatment approaches that arrest or reverse the caries process at a lesion level and reduce the loss of sound tooth structure. One of these approaches is the employment of caries arresting agents that possess antibacterial and remineralizing properties. Silver diamine fluoride (SDF) has drawn significant attention as an efficient caries arresting agent in children and adults. The major limitation with the use of SDF is the dark black staining of the carious tissue that compromises the esthetics. Silver ions are known for their antimicrobial effects, and silver nanoparticles (AgNPs) have the added advantage that it increases the surface area for exposure to the microbes. Literature reports that AgNPs have antimicrobial potential against predominant cariogenic flora. It has led to the development of nanosilver fluoride (NSF), a new colloid based on AgNPs, chitosan, and fluoride. It has shown to overcome the clinical limitations of SDF as it does not cause carious lesion staining. However, the current scientific literature lacks a comprehensive review of the benefits of using NSF for caries prevention and arrest. Thus, the purpose of this paper was to review the studies and clinical trials on NSF as a caries arresting agent, including antibacterial actions and modulation of the demineralization-remineralization balance.

Keywords: Dental Caries; Fluoride; Tooth Demineralization

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Received: 27 March 2021
Accepted: 05 May 2021
Online First: 05 May 2021

INTRODUCTION

Dental caries is the most prevalent oral disease that continues to affect almost every country in the world.[1] The contemporary dental practice focuses on non-restorative, non-invasive, and micro-invasive treatment approaches that arrest or reverse the caries process at a lesion level and reduce the loss of sound tooth structure. These treatment approaches include the employment of caries arresting agents, sealant, resin infiltration, fluoride varnish, fluoride toothpaste, and gel.[2–4]

Silver diamine fluoride (SDF), a metal ion-based topical fluoride solution, has drawn significant attention as an efficient caries arresting agent in children and adults.[5–8] Studies[9–13] have reported its effectiveness against cariogenic bacteria and fungi, and its remineralizing potential on enamel and dentin.[13–16] Major limitation with the use of SDF is the dark black staining of the carious lesions due to the precipitation of silver particles on the carious tissue.[17,18] Hence, its use in the aesthetic zone is not encouraging.[19–21] The other limitations of SDF use include; metallic taste, short-term staining to the skin which resolves in 2 to 14days[22] and mildly painful lesions on accidental contact of SDF solution with oral mucosa which generally heal within a couple of days.[6,23] To counter the undesirable staining, it is suggested to follow a combination protocol; potassium iodide (KI) application immediately after the use of SDF[17,24] or SDF mixed with glutathione(GSH) bio-molecule.[25]

The investigations on following the combination protocol revealed a positive effect in reducing the staining when compared to the use of SDF alone.[25–27] However, the use of KI has been associated with poorer caries control[28] and a certain degree of staining that can compromise the esthetics is observed in the carious arrested lesions.[24,26,29,30] Furthermore, the use of KI is contraindicated in pregnant women and during the first-six-months of breast-feeding because of the concern of overloading the developing thyroid with iodine.[22]

The advancement in nanotechnology led to the development of silver nanoparticles (AgNPs). The antibacterial properties of AgNPs have been well recognized in the medical field.[31,32] These particles are assumed more efficient due to their greater surface area that would increase the contact with microbial cells.[29] AgNPs have drawn attention from the dental researcher for their antibacterial potential that can be utilized in anti-caries approaches.[33]

Table 1 summarizes history and chronology of various silver compounds for caries management. Literature[12,34] reports that AgNPs have antimicrobial potential against predominant cariogenic flora. Furthermore, researchers have explored the combination of AgNPs and fluoride to include the advantages of each individual component.

Nano-silver fluoride (NSF), a new colloid based on AgNPs, chitosan, and fluoride was developed as a caries arresting agent that comprises both antibacterial and remineralizing properties.[30] Hence, NSF is a promising agent as it overcomes the clinical limitations of SDF as it causes no carious lesion staining.[29,30,35,36] This is due to the size of silver particles and also because the nanoparticles do not undergo oxidation.[29] This new formulation is safe for use in humans, and controlled clinical trials have shown its anti-caries property.[36–38] However, the current scientific literature lacks a comprehensive review of the benefits of using NSF in the treatment of dental caries. Thus, the purpose of this paper is to review NSF as a caries arresting agent, including antibacterial actions and modulation of demineralization-remineralization balance.

Table 1. History and chronology of various silver compounds for caries management

Year	Brief Description
1846[52]	The first recorded use of Silver Nitrate (SN) in the treatment of dental caries.
1891[53]	Reports have been made by Stebbins on the use of SN for dental caries inhibition. It has also been hypothesized that caries inhibition was due to bacterial-killing and the formation of a "black crust," which is a sclerotic protective coating of secondary dentin.
1902[52]	The first attempt has been made by Szabo to examine the penetration of SN in the dentinal tubules. It was found that SN penetrates through the whole carious lesion and into the sound dentin tissue. This penetration was not more than 0.5mm.
1905[54]	Miller proposed dentin protection against acids with the use of SN.
1917[55]	The first research director at Forsyth Institute in Boston, Perce Howe presented the modification of silver which was reduced from the solution with formalin and recommended its use for sterilization of the disintegrated dentin over the pulps. The solution penetrated the whole affected dentin but did not penetrate sound tooth tissue. He stated that the coagulation of the content of dentinal tubules gives dentin protection against the acids. After this, a renaissance began in the clinical use of SN.
1920s to 1930s[52]	'Howe solution' is used as a disclosing agent and bactericide in cavity preparation.
1941[52]	Zander HA published a histological investigation showing contrary results with the use of SN; The use of SN solution as a disclosing agent in dentin is considered doubtful. Because the bacteria were seen penetrating almost twice as far as the SN into the dentin. The use of SN as a disclosing agent for caries in enamel is of great value as it arrests caries for some time.
1940s to 1970s[56]	Five studies were published on the use of SN in the management of caries. Three of these studies showed no significant reduction in the incidence of caries when compared with no treatment. The other 2 studies evaluated caries arresting effect of SN solution.
1970s[53,57]	Developed silver diamine fluoride (SDF) to combine the actions of silver and fluoride. The combination showed its effects on the prevention and arrest of dental caries. This led to the approval of first SDF product, Saforide, Japan.
1980s[58–61]	The inhibitory effect of the combination of Silver and Fluoride on oral bacteria was assessed. Silver ion was shown to be the major inhibitor of oral bacteria. In clinical trials, another combination protocol was examined, using Silver fluoride followed by Stannous Fluoride(SnF_2). It showed to have synergistic effects in arresting caries lesions. Further, this combination had no adverse effect on permanent successors.
1990s[8]	SDF has been widely used in Brazil and Australia with in-vivo studies carried out in the respective countries to prevent and arrest dental caries.
2001 to 2013[6,11,16,49,62–69]	The anti-carious activity of SDF was investigated in several in-vitro studies. Hence SDF was documented to have antibacterial effects and remineralizing properties. Multiple randomized controlled clinical trials were carried out during the same time to evaluate the efficacy of SDF in preventing dental caries. It was found to be an effective non-invasive treatment approach in preschool children and schoolchildren. Clinical trials also document SDF to arrest root caries and prevent new root caries formation in elderly people.
2014[22]	The Food and Drug Administration(FDA) cleared SDF for use in the United States of America as a desensitizing agent.
2016[22]	SDF's off-label use was legally permissible and a CDT code had been approved for caries arresting medicaments to facilitate documentation and billing. The UCSF School of Dentistry Paradigm Shift Committee formed a subcommittee and developed a standardized guideline, protocol, and consent for the use of SDF.
2008[33]	AgNPs were used for caries control.

Table 1. Continued

2009 to 2019[33,70]	Researchers investigated AgNPs as an antimicrobial agent and confirmed it to inhibit the growth of cariogenic bacteria and biofilm adhesion. They were also found to preserve the collagen matrix and impede demineralization of enamel and dentin. AgNPs have been incorporated into dental materials for caries control. Sodium Fluoride(NaF) was combined with AgNPs to prevent and arrest caries. AgNPs were added to restorative materials such as restorative resin and adhesive systems with an intention to prevent secondary caries. Furthermore, AgNPs have been utilized in orthodontics accessories such as brackets, elastomeric ligatures, adhesives, and removable retainers.
2014 to 2020[29,30,35,48]	Multiple studies have investigated the antibacterial properties of NSF. The AgNPs in the formulation have the added advantage that it increases the surface area for exposure to the microbes. It has shown to inhibit cariogenic bacterial growth and biofilm adhesion and cause bactericidal actions without harming human cells. Studies confirm effective remineralizing properties of NSF on both the primary and permanent tooth. NSF has shown to be a simple, inexpensive, non-toxic, non-invasive caries arresting agent, and it did not present carious lesion staining.

Mechanism of action of NSF

The antibacterial properties of nanomaterials have been investigated, and the antibacterial effect showed to come from AgNPs. Although the exact mechanism of antibacterial action of AgNPs has not been entirely understood, several antibacterial actions have been proposed and elaborated in Figure 1. Chitosan was added to the AgNPs as it acts as a carrier and stabilizes the compound. Further, to make this a more comprehensive agent, fluoride was added to the AgNPs-chitosan compound to fortify the antibacterial properties and prevent demineralization. This new formulation, called NSF, has been reported for caries prevention and arrest.[33]

Antibacterial properties of NSF

Streptococcus mutans (SM) are the primary cariogenic bacteria, and they are associated with the initiation and progression of carious lesions. The oral bacteria exist collectively in the extracellular matrix to form a biofilm, which increases the resistance of microorganisms to antibacterial agents. Table 2 summarizes five in vitro studies and one clinical trial investigating the antibacterial effect of NSF on cariogenic bacteria.

Studies[39,40] have shown that the antibacterial activity of AgNPs increases with a decrease in their particle size. Accordingly, few studies have shown AgNPs in the range of 2.56 ± 0.43 nm, 3.2 ± 1.2 nm and 5.9 ± 3.8 nm in NSF formulations to favour the antibacterial activity against SM.[35,38,41] Sodium borohydride has been regularly used as a reducing agent in preparing NSF formulations.[38,41,42] However, due to concerns over toxicity, some researchers have used thiolated polyethylene glycol (PEG) as both a reducing agent and a capping agent for its preparation. Several advantages have been reported for the use of PEG; it increases AgNPs stability to a level that they can be preserved at high ionic concentrations, PEG-coated AgNPs have shown to be less toxic than those with other capping agents and are less liable to oxidize.[35] Comparison between NSF and SDF for minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) values showed better results with the NSF. Cytotoxicity assessment by hemolytic activity showed NSF to be less toxic to human erythrocytes than SDF. Another study by Yin et al.[35] showed half-maximal inhibitory concentration (IC50) of PEG-AgNPs against SM to be half of IC50 against human gingival fibroblasts (HGF-1). This indicates the provision of bactericidal action without harming human cells. NSF showed greater anti-adherence and anti-acidogenicity effects against SM when compared to sodium fluoride (NaF).[43] NSF has been suggested as an effective SM biofilm inhibitor because it has shown to reduce the CFU counts and dental biofilm inhibition values.[30,42–44] Thus, NSF formulation can act as a more biocompatible antibacterial agent against SM.

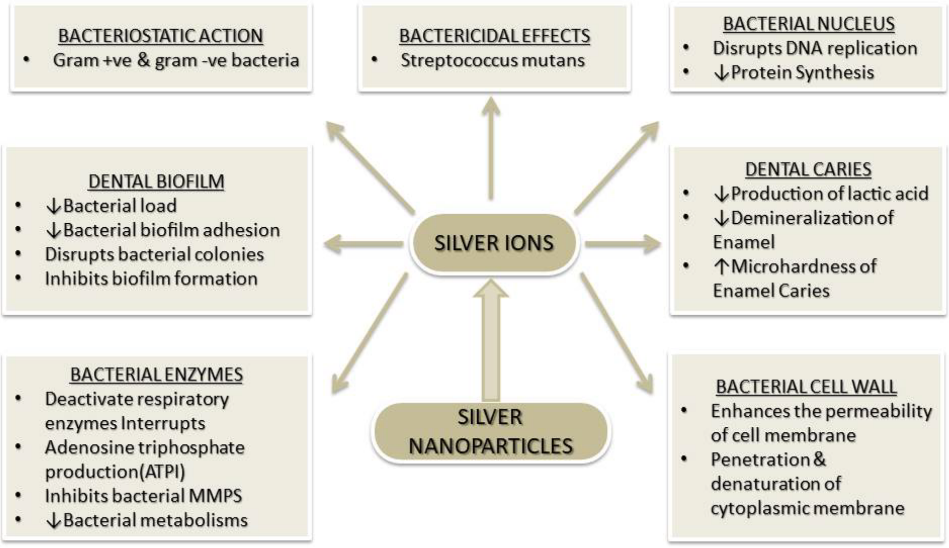

Figure 1. Mechanism of action of silver nanoparticles

Remineralizing properties of NSF

Table 3 summarizes seven laboratory studies that have evaluated the NSF effectiveness in remineralizing enamel and dentin of primary and permanent teeth. NSF formulation was compared with NaF for primary tooth enamel remineralization and it showed remineralizing effect similar or greater to NaF.[42,43,45,46] In a study by Akyildiz et al.[47] comparison of NSF with SDF and NaF showed that all the three remineralizing agents were statistically significant in rehardening the artificially demineralized enamel specimens of third molars. However, NSF was not shown to be as effective as SDF and NaF. SDF (12%) and NSF formulation (2.5% NaF with PEG-AgNPs) have shown similar effects for dentine caries remineralization and collagen degradation inhibition.[48] In a study by Sayed et al.[30] SDF has shown to cause distortion in the dentin collagen morphology but provides an intrafibrillar pattern of mineral deposition. However, NSF showed to preserve collagen structural morphology and provides intrafibrillar remineralization. The change in the collagen fiber morphology has been related to the high pH of SDF (pH 10-12) compared to NSF (pH 8-9). This indicates better biocompatibility with the use of NSF and it can be an alternative agent for SDF.

Clinical trials on the effectiveness of NSF in arresting dental caries

Table 4 summarizes four clinical trials that investigated the effectiveness of NSF formulations in preventing and arresting caries in children. Tirupathi et al.[36] have compared caries arresting efficacy of NSF preparation and SDF on an annual application in primary molars. It showed a 77% success rate with NSF preparation compared to 71.05% success in the SDF group. Although the success rate was comparatively better in the NSF group than the SDF group, the difference was not statistically significant. In a study by Santos et al.[38], NSF formulation has shown the results(66.7%) of caries arrest similar to that of SDF as reported in the clinical trial by Llodra et al.(6) (>55%) but was lower than the outcome reported by Chu et al.[49] (>96%) This was due to difference in the trial design and intervals of application. However, they both have shown to be effective in arresting dental caries.[38] Another study by Nagireddy et al.[50] has shown 65.21% effectiveness with NSF formulation in arresting caries after 12 months of follow up; this was comparable to 67% NSF results reported in the clinical trial by Santos et al.[38]. NSF application is a simple, inexpensive approach that requires no comprehensive dental clinical setup and can be affordable by most communities.

Table 2. Studies on antibacterial properties of nanosilver fluoride

Study and its design	Characteristics and Summary Intervention	Study Findings
Sayed M et al, 2020[30] In-vitro study **Test Microbe: SM**	1) Sample: 25 demineralized dentin specimens 2) Distribution: 5 groups (n=5); i) SDF, ii) AgNPs/KF, iii) KF, iv) AgNPs, v) Control. 3) Outcome measures: i) Measurement of regeneration potential of SM through CFU values, ii) Assessment of bacterial growth inhibition through optical density	NSF preparation (AgNPs/KF) has shown to possess effective antibacterial properties
Yin IX et al, 2020[35] In-vitro study **Test Microbe: SM**	1) Antibacterial and cytotoxic effect of PEG-AgNPs against SM and HGF-1 vs $AgNO_3$ (comparator), and SDF (positive control) through IC50 values 2) Antibacterial effects (IC50 values) of 4 fluoridated PEG-AgNPs solutions containing various ratios of PEG-AgNPs (12800, 6400, 1600, and 400 ppm Ag) and NaF (fixed at 2.5% = 11,310 ppm F)	PEG-AgNPs have shown to inhibit the growth of SM. Solution with the combination of NaF and PEG-AgNP showed no synergistic antibacterial effect but provides a therapeutic window for fine-tuning of each component's ratio and concentration to inhibit SM without harming the human cells.
Silva et al, 2018[43] In-vitro study **Test Microbe: SM**	1) Sample: 27 enamel fragments of primary teeth. 2) Distribution: 3groups(n=9); i) NSF (Experimental group), ii) NaF (positive control), iii) Deionized water(negative control) 3) Outcome measures: i) Acidogenicity - % pH variation, ii) Quantification of bacterial adherence through CFUs and subsequent % bacterial adsorption inhibition.	NSF was found more effective in preventing pH decline and bacterial adhesion in comparison with NaF.
Teixeria et al, 2018[42] In-vitro study **Test Microbe: SM**	1) Distribution: 3groups; i) NSF containing dentifrices (test dentifrice), ii) NaF containing dentifrices (positive control), iii) Deionized water (negative control). 2) Outcome measures: i) MIC, ii) MBC, iii) % bacterial adsorption inhibition, iv) Acidogenicity - % pH variation	NSF containing dentifrices have shown better antibacterial effect compared to NaF containing dentifrices.
Freire PLL et al, 2017[44] A randomized, pilot clinical trial study ***Duration:*** **Test Microbe: SM**	1) Sample: 12 schoolchildren of both genders, aged:7-8yrs. 2) Distribution: 2groups; i) NSF, ii) control (saline solution). 3) Outcome measures: i) Biofilm pH measurement, ii) Bacterial growth measurement by spectrophotometry, iii) OHI-S, iv) Bacterial count through CFU.	NSF has shown to reduce SM growth and presented as an effective means to inhibit dental biofilm formation.
Targino et al, 2014[41] In-vitro study **Test Microbe: SM**	1) NSF vs [CHX and SDF] (Control solutions) 2) Outcome Measures: i) Antibacterial activity through MIC and MBC ii) Cytotoxicity through hemolytic activity in human erythrocytes.	NSF showed as an effective antimicrobial agent similar to SDF. NSF has shown lower toxicity to living cells when compared to SDF.

Table 3: In vitro studies on remineralizing properties of nanosilver fluoride

Study and its design	**Characteristics and Summary Intervention**	**Study Findings**
Sayed M et al, 2020[30]	1) Sample: 25 Dentin specimens from bovine incisor roots. 2) Distribution: 5 groups (n=5); i) SDF, ii) AgNPs/KF, iii) KF, iv) AgNPs, v) Control. 3) Outcome measure: Transmission electron microscopy	NSF preparations have preserved dentin collagen, whereas, SDF has shown to alter dentin collagen morphology
Zhao IS et al, 2020[48]	1) Sample: Extracted sound third molars. 2) Distribution: 18 dentine slices cut into 54 blocks which were divided into 3 groups(n=18); i) Group 1 - SDF, ii) Group 2 - PEG-AgNPs with NaF, iii) Group 3 - Deionized water. 3) Outcome measures: i) SEM: surface morphology and cross-sectional features, ii) Spectrophotometry: collagen degradation, iii) XDR: crystal characteristics.	NaF solution with PEG-AgNPs showed a similar effect to SDF in remineralizing artificial dentine caries and inhibiting collagen degradation.
Akyildiz et al, 2019[47]	1) Sample: 45 humans third molars 2) Distribution: 180 enamel specimens were divided into 4groups; i) NSF, ii) SDF, iii) NaF, iv) control. 3) Outcome measures: i) VHN, ii) SEM.	NSF was not found comparatively effective as NaF varnish and SDF on enamel caries lesions.
Silva AV et al, 2019[45]	1) Samples: 33 primary tooth specimens 2) Distribution: 3groups (n=11); i) G1-NSF(experimental), ii) G2-NaF(positive control), iii) G3-No remineralizing agent(negative control) 3) Outcome measure: OCT	NSF is as efficient as NaF for enamel remineralization in primary teeth.
Teixeria et al, 2018[42]	1) Sample: 48 primary molars 2) Distribution: 3groups (n=16units); i) NSF containing dentifrices (test dentifrice), ii) NaF containing dentifrices (positive control), iii) Deionized water (negative control). 3) Outcome measures: Microhardness test, OCT	NSF is as effective as NaF for enamel remineralization in primary molars.
Silva et al, 2018[43]	1) Sample: primary tooth enamel fragments. 2) Distribution: 33 samples into 3groups (n=11); i) NaF(positive control), ii) NSF (experimental group), iii) Deionized water(negative control) 3) Outcome measures: Microhardness test, Fluorescence spectroscopy and OCT	NSF is as efficient as NaF for primary tooth enamel remineralization.
Nozari A et al, 2017[46]	1) Sample: 80 sound primary anterior teeth 2) Distribution: 60 samples into 4 groups (n=15); i) NSF, ii) NaF varnish, iii) n-HAP, iv) Control(no treatment) 3) Outcome measures: SMH, AFM	NSF can have greater remineralizing capability than NaF varnish and n-HAP for primary anterior teeth

SDF: Silver diamine Fluoride; NSF: Nanosilver fluoride; AgNPs: Silver nanoparticles; KF: Potassium fluoride; PEG-AgNPs: polyethylene glycol-coated silver nanoparticles; NaF: Sodium fluoride; SEM: scanning electron microscopy; XDR: X-ray diffraction; VHN: Vickers microhardness; OCT: Optical coherence tomography; n-HAP: Nano-Hydroxyapatite serum; SMH: Surface microhardness; AFM: Atomic Force Microscopy.

Table 4. Clinical trials assessing the effectiveness of nanosilver fluoride in arresting dental caries

Study	Characteristics and Summary Intervention	Study Findings
Nagireddy VR et al, 2019[50] Duration:1year	1) Sample: 60 children of the 4-9years age range 2) Distribution:100 primary molars were divided into 2 groups; i) NSF - experimental group, ii) Saline - control group 3) Follow up: after 7days, 5months and 12months	NSF has shown to be an anticaries agent and presents a non-invasive option for arresting dental caries in children
Tirupathi et al, 2019[36] Duration:1year	1) Sample: 50 school children aged between 6-10years. 2) Distribution: 159 primary molars were divided into 2 groups. i) NSSF - experimental group, ii) SDF - positive control 3) Follow up: 1month, 3months, 6months and 12months.	An annual application of NSSF showed similar efficacy as SDF in arresting dentinal caries in primary molars.
Burns J, Hollands K, 2015[37] Duration:1year	1) Sample: 60 children with 6.31 (± 0.60) mean age range 2) Distribution:130 primary molars were divided into 2 groups; i) NSF - experimental group, ii) Saline - control group 3) Follow up: 1week, 5month, 1year	An annual application of NSF solution has shown to be effective in hardening and arresting dentine caries in primary teeth.
Santos et al, 2014[38] Duration:1year	1) Sample: 60 school children of a poor community with a mean age of 6.31± 0.60 years. 2) Distribution: 130 primary teeth were divided into 2 groups(n=65). i) NSF - experimental, ii) Water - control 3) Follow up: 1week, 5months, and 12months.	NSF has shown to be an effective caries arresting agent for children in poor communities.

NSSF: Nanosilver incorporated sodium fluoride; SDF: Silver diamine Fluoride;

NSF vs SDF on caries lesion staining

Table 5 summarizes 4 in-vitro studies assessing the staining effects of NSF. The staining phenomenon with SDF application is due to the silver particle's precipitation and their oxidation on the carious dentin.[17,18] Contrary to this, NSF formulations do not form oxides when coming in contact with the medium's oxygen and hence does not cause dentin staining.[38] The study by Sayed et al.[30] showed that no colour change observed over time with the reduction in the size of AgNPs. Another study by Espíndola-Castro et al.[29] showed that 2 weeks after the NSF application, yellowish stains were seen on the teeth. The chitosan in the composition of NSF formulation is believed to be the cause of this stain formation. However, these stains were removed later by toothbrushing, and the tooth colour restored to the baseline values. The authors also observed that this staining could also be removed easily with a gauze. The precise quantification of different colour characteristics carried out in other studies with an objective instrumental measurement approach. It revealed that fluoridated polyethylene glycol-coated silver nanoparticles (PEG-AgNPs) showed no observable dentin staining. The dentin discolouration displayed with SDF application was not acceptable clinically as it was more than ten times higher than the acceptable upper threshold.[35,48,51] Therefore, the NSF formulations have been suggested as a better alternative for caries arrest to overcome the staining disadvantage of SDF.

Table 5. Nanosilver fluoride and silver diamine fluoride

Study	Characteristics and Summary Intervention	Study Findings
Espíndola-Castro et al 2020[29]	1) NSF formulations(600 and 1500ppm) vs other commercially available cariostatic agents (Advantage arrest, Riva star and cariestop) 2) Sample & Distribution: 75 extracted human molars were divided among 5 cariostatic agent(n=15) 3) Spectrophotometric analysis: i) Before application, ii) After 2weeks, iii) After 4weeks.	NSF formulations can be an alternative to SDF as they do not compromise esthetics.
Sayed M et al, 2020[30]	1) SDF vs KF vs AgNPs vs AgNPs/KF(Nano silver/potassium fluoride) 2) Sample & Distribution: 100 bovine dentin specimens and divided among 5groups i) SDF, ii) AgNPs/KF, iii) KF, iv) AgNPs, v) Control. 3) Spectrophotometric analysis: i) Before surface treatment, ii) Immediately after surface treatment and after, iii) 1 day, iv) 2 days, v) 7days.	NSF preparation can be an alternative to SDF as it shows no colour change over time
Yin IX et al, 2020[35]	1) NaF(2.5%) solutions with PEG-AgNPs at 12,800, 6400, 1600, and 400 ppm vs 38% SDF(positive control) vs water(negative control) 2) Sample & Distribution: Extracted sound human 3rd molars have been selected and 18 dentin slices were prepared for evaluation using a dental spectrophotometer.	PEG-AgNPs to NaF have not shown any staining effect, whereas SDF application resulted in obvious black staining.
Zhao IS et al, 2020[48]	1) SDF vs NaF with PEG-AgNPs vs Deionized water(negative control) 2) Sample & Distribution: Extracted sound human 3rd molars; 12 dentin blocks were allocated to each group for evaluation using a dental spectrophotometer.	Fluoridated PEG-AgNP does not stain dentin caries and hence it could be a better alternative to address the disadvantage of SDF.

SDF: Silver diamine Fluoride; NSF: Nanosilver fluoride; AgNPs: Silver nanoparticles; KF: Potassium fluoride; PEG-AgNPs: polyethylene glycol-coated silver nanoparticles; NaF: Sodium fluoride.

CONCLUSIONS

NSF is a simple, inexpensive, non-toxic, non-invasive approach for arresting dental caries. It presents as an effective caries arresting agent that possess antibacterial actions of AgNPs and remineralizing properties of fluoride. It does not stain the carious lesion and hence showed to overcome the major limitation with SDF use.

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How to cite this article:

Mohammed Zameer, Sameen Badiujjama Birajdar, Syed Wali Peeran, Syed Nahid Basheer, Syed Ali Peeran, and Arun Reddy. Nanosilver fluoride as a caries arresting agent: A narrative review. Contemp Pediatr Dent 2021:2(1):1-13

Declarations

Acknowledgements: *Not applicable.*

Conflict of Interest Statement: *The authors disclose no potential conflicts of interest.*

Ethics Statement: *This study does not require approval from the ethics committee.*

Informed Consent: *Not required.*

Author contributions: *Conception and design: MZ; Acquisition of data: MZ, SNB; Interpretation of data: MZ, SWP; Drafting article: MZ, SBB, AR; Revision artice: SBB, SNB, SAP, AR; Final approval: All Authors*

Funding: *This work is not finantiated.*

Data Availability: *The data used to support the findings of this study can be made available upon request to the corresponding author.*

Peer-review: *Externally double-blinded peer-reviewed.*