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Dr. Prasurjya Bora
Post Graduate, Department of Pediatric & Preventive Dentistry, ITS Dental College, Greater Noida, Uttar Pradesh, India

Dr. Tanu Nangia
Professor, Department of Pediatric & Preventive Dentistry, ITS Dental College, Greater Noida, Uttar Pradesh, India

Dr. Aditya Saxena
Reader, Department of Pediatric & Preventive Dentistry, ITS Dental College, Greater Noida, Uttar Pradesh, India

Dr. Tenzin Kunchok
Post graduate, Department of Pediatric & Preventive Dentistry, ITS Dental College, Greater Noida, Uttar Pradesh, India

Dr. Aayushi Sangal
Post graduate, Department of Pediatric & Preventive Dentistry, ITS Dental College, Greater Noida, Uttar Pradesh, India

Corresponding Author:
Dr. Prasurjya Bora
Post Graduate, Department of Pediatric & Preventive Dentistry, ITS Dental College, Greater Noida, Uttar Pradesh, India

Silver diamine fluoride: Role in management of dental caries

Dr. Prasurjya Bora, Dr. Tanu Nangia, Dr. Aditya Saxena, Dr. Tenzin Kunchok and Dr. Aayushi Sangal

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Abstract
Dental caries is a multifactorial disease affecting children and adults alike all over the globe. The patients with dental caries present with various symptoms depending on the extent of carious involvement. It initially presents as a white-spot lesion which, if left untreated, may demineralize the tooth structure, thereby compromising the pulp. To combat the rising problems associated with dental caries, Silver Diamine Fluoride (SDF) has come as a game changer in the field of dentistry. It is a colourless solution which contains silver as an antimicrobial as well as fluoride to help in the prevention and arrest of dental caries. The fluoride penetrates deeper into the tooth with SDF as compared with other fluoride solutions, creating a fluoride reservoir in the tooth structure. SDF has been recently approved by the US Food and Drug Administration as a dentin desensitizer but is also used to treat carious lesions. The advantages it has over other fluoride agents is because of its high efficiency and no requirement of any instrumentation to remove the lesion, thus making it a widely accepted method of caries control.

Keywords: Silver diamine fluoride, dental caries, children and adults

Introduction
Minimal intervention dentistry is a concept of dental treatment that is concerned with the causes of dental diseases and doesn't emphasize only on the symptoms of the disease. The ideology of minimal intervention dentistry involves the prevention of disease and preservation of the integrity of the tooth structure [1]. With the increase in the understanding of caries progression and the introduction of adhesive restorative materials, the concepts of minimal intervention dentistry have evolved; the core being earliest detection and prevention of disease, succeeded by less invasive treatments. It emphasizes on the pin-point excision of dental tissues without any mutilation of the adjacent tissues [2].
The World Dental Federation has proposed a policy in which there are some basic principles that are to be applied to meet the requirements of minimal intervention dentistry3 –

1. Controlling the diseases by reduction in cariogenic oral flora.
2. Achieving remineralization of early lesions by performing minimally intervening procedures.
3. Repairing instead of replacing defective restorations.

Rather than being exclusively restorative, minimal intervention dentistry is also based on biological solutions. It comprises of 3 stages of prevention [4]:
Primary prevention – Mainly emphasizes on the elimination of new cases of oral diseases. It can be achieved by methods such as water and salt fluoridation, increasing public awareness on dental diseases, proper oral hygiene habits and also on the detrimental effects of cariogenic diet on the teeth.
Secondary prevention – Aims at detection of disease progression rate to establishment of caries in the teeth by various screening tests so as to arrest the progression of the lesion at the earliest and thereby providing suitable treatment modalities.
Tertiary prevention – Focuses on the prevention of recurrence of the disease and also the negligence of previous preventive and restorative treatments provided.

In the past, clinicians have abided by G.V Black's cavity design and the principle of ''extension for prevention'' surgical approach for the management of aggressive oral diseases [5]. This concept was based on the fundamentals of removing all the demineralized areas of the tooth followed by a restoration that would occlude the cavity. With the introduction of ultra-high-speed rotary cutting instruments in the 1950s, there was a distinct increase in replacement dentistry. As a result, a substantial amount of tooth structure was removed, often more than only the demineralized part in the process of restoring a carious tooth. Hence the structural integrity of the tooth was compromised [6].

However, in the recent times the principle has changed into "prevention of extension" for the surgical management of carious lesions with the introduction of minimal intervention dentistry. With the advancement of technology and dental materials, it has become comparatively easier and more convenient to identify and heal early lesions [7]. Right from remineralizing agents to chemomechanical cavity preparation to air abrasion, ozone therapy and resin infiltration, minimal intervention dentistry has come a long way into the modern-day dental practice.

In recent times, many studies have shown satisfactory results when assessing carious lesions treated by considering its clinical, ultrastructural, microbiological and chemical aspects [8, 9, 10, 11, 12, 13]. It has been seen that after partial removal of carious dentine and the hermetic sealing of cavities, there is a decrease in bacterial growth, absence of microorganisms or inactivation. Thus, there would be no progression of the carious lesion [10, 11, 12, 13].

To reduce the burden of caries disease in young children and to avoid possible serious consequences of untreated decay, it is important to identify an effective, low-cost method of treating caries in children who are at high risk and with limited access to dental care. A tooth with a deep carious lesion approximating the pulp but without signs or symptoms of pulp degeneration should be dealt with using a minimally invasive approach in which the soft carious dentin is removed followed by the placement of a suitable medicament which has the ability to remineralize the tooth structure. This atraumatic approach helps in minimizing psychological trauma to the child and anxiety related to local anesthesia and conventional full cavity preparation.

Silver diamine fluoride (SDF) in a concentration of 38% has been identified as one such anticariogenic agent that successfully arrests dental decay and has the potential to address the epidemic of untreated decay in young children [14]. It is an alkaline based, colourless solution which forms complex with ammonia and has silver particles for antimicrobial properties as well as fluoride to prevent and arrest caries. It has an ability to halt caries progression and prevent the development of new caries simultaneously [15]. In 2014, SDF was cleared by the US Food and Drug Administration for hypersensitivity[16]. The use of SDF as a preventive or therapeutic modality can prevent or delay dental treatment until a child reaches a more cooperative age; therefore, serving as a nonsurgical alternative to managing caries in populations where surgical management of decay is not an option [17]. It has the ability to effectively arrest decay in carious lesions that were easily clinically detectible. It offers an easy, highly efficient, and well-accepted nonsurgical alternative treatment for early childhood caries in young children rather than traditional restorative dental treatment [18]. Thus, Silver Diamine Fluoride appears to be a useful immediate treatment for children who can't receive traditional restorative treatment for dental decay and therefore can be widely implemented for caries control to meet patient needs.

Courtesy: elevateoralcare.com

Fig 1: IMG: Advantage Arrest

Discussion

The introduction of minimally invasive dentistry has changed the whole concept of dealing with carious lesions from ''extension for prevention'' to "prevention of extension". As a result, less invasive non-surgical approach to manage dental caries have emerged thereby promoting various chemotherapeutic procedures. In this era of atraumatic dentistry, SDF has emerged as a game changer in the management of dental caries and its complications. SDF not only halts the progression of caries but also helps in remineralizing the lost tooth structure over time, making it one of the most efficient tools.

Conventional treatment of early childhood caries in young children involves drilling and filling which evokes many challenges like behavioral issues and lack of cooperation. Hence, majority of patients are left untreated, which ultimately results in early loss of teeth [19, 20]. Loss of deciduous teeth mainly upper anteriors appear unaesthetic and may cause psychological trauma to the patient or phonation problems. Primary teeth also play a vital role in the normal development and growth of jaws along with prompt eruption of the permanent teeth. Hence, with the implementation of silver diamine fluoride, caries can be arrested, and above-described problems can be overcome.

Bactericidal activity of silver ion has been known since ancient times around 1000 B.C. (Russell and Hugo, 1994). In 1846, the first reported use of silver nitrate was to tackle erosion. When applied directly on to a carious lesion, it prevented the advancement of carious lesions. Stebbin in 1891, documented that teeth filled with amalgam gave away blackish discoloration on the surfaces, while promoting cessation of caries. Japan was the first country to approve SDF for its use as a therapeutic agent in the 1960s [21, 22]. Since then, SDF has been on the international market for over 40 years now and in 2014, the United States Food and Drug Administration (FDA) cleared the use of SDF in treating dental diseases [16]. SDF is a colorless liquid with a pH of 10, with a concentration of 24.4-28.8% (253, 870 ppm) volume of

silver, 5.0-5.9% fluoride (44,800 ppm), and ammonia [14]. Fung *et al*., have reported that the fluoride ions in SDF act predominantly on tooth structure while the silver phosphate component acts against the cariogenic bacteria inhibiting dentinal collagen degradation. It reacts with the enamel hydroxyapatite and results in the formation of fluorapatite, which has been shown to be more caries resistant than hydroxyapatite in an acidic environment [23]. Furthermore, it has shown to be safe for the pulp by not inciting pulpal inflammation or necrosis and promoting the formation of tertiary dentin [24].

Fig 2: IMG Advantage Arrest

Mechanism of action: SDF also has antibacterial properties. Silver ions bind with negatively charged peptidoglycans in bacterial cell walls and disrupts the membrane transport function, which in turn leads to cellular distortions and loss of viability [25]. Binding to sulphydryl groups (thiol group of cystine), which is essential for enzyme activities, can inhibit bacterial enzyme activities, disrupt metabolic processes, and eventually cause death of the microbe [26, 27, 28]. On the other hand, sodium fluoride reacts with calcium phosphate forming fluorapatite which increases the dentin microhardness making it resistant to microbial interaction and sodium hydroxide thereby initiating a basic environment. Ammonia plays an important role in keeping the solution at a constant concentration for a certain period of time. Moreover, bacteria killed by the silver particles incite a 'zombie effect' where the active bacteria are killed upon contact with the silver-affected bacteria [29]. *In vitro* studies have demonstrated that SDF increases the pH of biofilm, reduces dentin demineralization, and has antimicrobial action against cariogenic bacteria [15]. However, the teeth treated with SDF sometimes establish black stains due to the effect of silver phosphate precipitation [14]. Other studies suggested that silver fluoride regimens inhibit Streptococcus mutans growth and penetrate enamel to a depth of 25 microns [30], and that approximately two to three times more fluoride is retained than that delivered by sodium fluorophosphates (NaF-PO4), sodium fluoride (NaF), or stannous fluoride (SnF2).

The overall reaction can be summarized as

$Ca_{10}(PO_4)6(OH)^2 + Ag(NH_3)2F = CaF2 + Ag_3\ PO_4 + NH4\ OH$

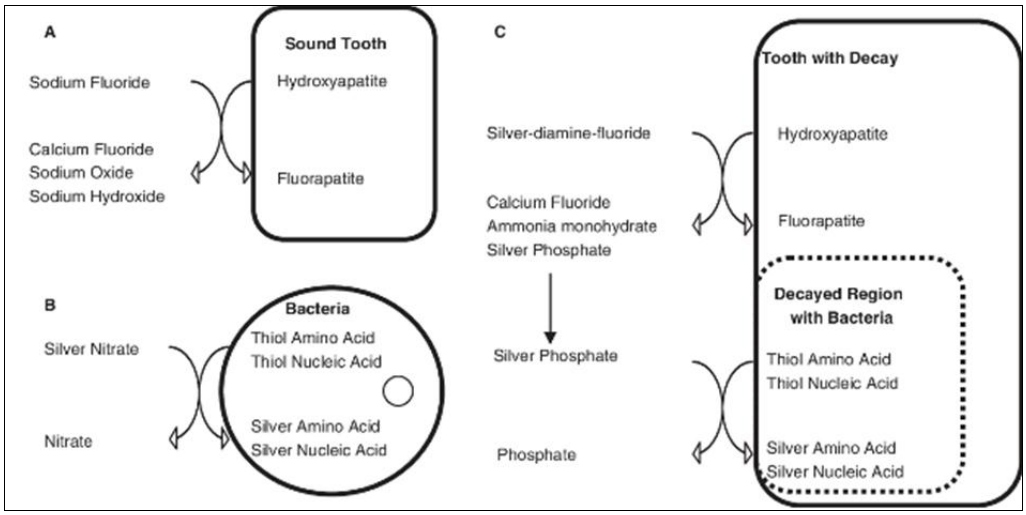


Fig 3: Courtesy of: Rosenblatt, A., Stamford, T. C. M., & Niederman, R. (2009). Silver Diamine Fluoride: A Caries "Silver-Fluoride Bullet." Journal of Dental Research, 88(2), 116–125. doi:10.1177/0022034508329406

Effect on cariogenic bacteria: Teeth which are treated with SDF seem to have lower S. Mutans count than those teeth which are not treated with SDF [31]. It is available in various concentrations such as 38%, 30% and 12% out of which 38% is the most effective [32, 33]. The 38% SDF contains high concentrations of silver ions that inhibit biofilm formation by restricting polysaccharide synthesis by the bacteria [34]. Fluoride also acts on the inhibition of biofilm formation by binding onto the bacterial cells and can modify enzymes such as proton-extruding adenosine triphosphate. These enzymes are known to prevent the metabolism of carbohydrates by the acids produced by cariogenic bacteria [35]. The antimicrobial efficacy of SDF is more profound in mono-species of S.Mutans than dual-species biofilm. It may be due to the cell-to-cell communication of both the species leading to alteration in the composition of the bacterial cell wall polysaccharides and may slowly inhibit the antimicrobial penetration power [33]. Furthermore, repeated application of SDF after one week will enhance its antimicrobial efficacy.

Effect of SDF on mineral content of enamel and dentine: After application of SDF on a demineralized tooth surface, it was found that it inhibits the progression of the lesion deeper into the dentine and the surface microhardness of these treated lesions, up to a depth of 150um approximately [36, 37, 38, 39, 40]. It also promoted the absorption of calcium and inhibited its dissolution from the enamel [38, 41, 42]. Elemental analysis performed in a study reported that the concentrations of calcium and phosphorus in demineralized dentine treated with SDF were significantly higher than those of calcium and

phosphorus in demineralized dentine without SDF treatment. Besides, it also prevents loss of minerals from the demineralized tooth surfaces [36, 37]. Another study reported the formation of a highly mineralized zone abundant in calcium and phosphate in arrested carious lesions treated with SDF [43].

Effects of SDF on the organic content of dentine: Tooth surfaces treated with SDF show a large amount of intact collagen which increases dentin bond strength.[44] Matrix metalloproteins, such as MMP-2, MMP-8 and MMP-9 which have a degrading effect on the dentin surfaces are found to be inhibited by SDF [45]. It acts by inhibiting the proteolytic activities of these enzymes thereby prohibiting the breakdown of collagen [46].

SDF as a non-restorative treatment: In situations where carious lesions cannot be managed by caries removal and restoration such as in the case of inadequate remaining tooth structure or lack of patient cooperation or in the case of pediatric patients where there is a need to allow the child to accommodate to the dental environment, SDF can play a very significant role due to its ease of application and reduced chair time. It gives the patient time to make changes in their oral hygiene behavior and diet and thus allows the inhibition of disease progression [47].

SDF as desensitizing agent for sensitive teeth: Upon application of Silver diamine fluoride, a squamous layer is formed on the dentinal surface which thereby occludes the dentinal tubules. Hence, silver diamine fluoride can be applied on to hypersensitive dentin. In a lesion like erosion or abrasion, any kind of mechanical or thermal stimuli will elicit dentinal hypersensitivity. Therefore, application of silver diamine fluoride can be an effective alternative treatment.

SDF as a restorative treatment: SDF can also be used as an adjunct to restorative treatment by its application on the carious tooth surface followed by the placement of a restoration. It can therefore be used along with atraumatic restorations [48] (also known as Silver Aided ART or SMART) [49, 50] (figure 1) or with Hall technique. It can be done immediately after placing SDF or waiting for a few days or weeks post application of SDF till the carious lesions are arrested. It can also be used for treating dentinal hypersensitivity and symptomatic molar incisor hypomineralization (MIH). The silver ions present in SDF have the potential to occlude dentinal tubules by producing calcium fluoride and silver iodide [51].

Indications and Contra-indications of SDF:

Indications:

- Asymptomatic cavitated dentine carious lesions in primary teeth
- Cleansable lesions
- Unrestorable dentinal lesions
- Anxious patients who have a fear of invasive treatment
- Carious lesions requiring multiple visits
- Root surface carious lesions (primary and permanent teeth)
- Patients with high caries risk with medical or psychological conditions
- Non-carious cervical lesions giving sensitivity
- Molar incisor hypomineralization to reduce sensitivity
- Patients with good oral hygiene practice
- Recurrent Caries at restoration margins
- Incipient interproximal lesions

Contraindications

- Patients with ulceration, mucositis, stomatitis.
- Patients with allergy to silver, fluoride or ammonia
- Clinical signs or symptoms of irreversible pulpitis, or dental abscess/fistula
- Radiographic signs of pulpal involvement, or peri-radicular pathology
- Infection or pain from pulp or food packing (unless shape of tooth can be changed to become cleansable)
- Active carious lesions
- Patients with poor oral hygiene habits
- Pregnant or breastfeeding women
- Patients undergoing thyroid gland therapy or on thyroid medication
- Patients with known allergy to potassium or iodine.

Clinical application of SDF (According to AAPD)

- Gross debris is to be removed from the cavity to allow SDF to be in contact with denatured dentin.
- Carious dentin excavation before application of SDF is not indicated as excavating the lesion may reduce proportion of arrested caries lesions that become black, it may be considered for esthetic purposes.
- A protective coating of petroleum jelly may be applied to the lips and skin of the oral mucosa to prevent a temporary henna-appearing tattoo that can occur if soft tissues come into contact with SDF.
- Isolate areas to be treated with cotton rolls, rubber dam or other isolation methods. If applying cocoa butter or any other product to protect surrounding gingival tissues, use care not to unintentionally coat the surfaces of the caries lesions.
- Upon applying SDF on primary teeth adjacent to permanent anterior teeth that may have non-cavitated (white spot) lesions, proper caution must be taken to avoid staining the permanent teeth accidentally.
- Careful and precise application with a microbrush should be adequate to prevent intraoral and extraoral soft tissue exposure. No more than one drop of SDF should be used for the entire appointment.
- Allow a gentle flow of compressed air to dry the lesion.
- Bend the micro sponge brush into SDF and dab on the side of the plastic dappen dish to get rid of excess liquid before application. Apply SDF directly to only the affected tooth surface. Remove excess SDF with gauze, cotton roll, or cotton pellet to minimize systemic absorption.
- Application time should be of at least one minute if possible. (Application time likely will be shorter in very young and difficult to manage patients. When using shorter application periods, monitor carefully at post-operative and recall visits to evaluate arrest and consider reapplication.)
- A gentle flow of compressed air is applied until medicament is dry. Try to keep the lesion isolated for as long as three minutes.
- The entire dentition may be treated after SDF treatment with five percent sodium fluoride varnish to help prevent caries on the teeth and sites not treated with SDF.

Follow-up (According to AAPD)

Estimations of SDF effectiveness in arresting dental caries lesions range from 47 to 90 percent with one-time application depending on size of the cavity and tooth location. Anterior teeth have higher rates of arrest than posterior teeth. Therefore, follow-up for evaluation of caries arrest is advisable.

- Follow-up at 2-4 weeks after initial treatment to check the arrest of the lesions treated.
- Reapplication of SDF may be indicated if the treated lesions do not appear arrested (dark and hard). Additional SDF can be applied at recall appointments as needed, based on the color and hardness of the lesion or evidence of lesion progression.
- Caries lesions can be restored after treatment with SDF.
- When lesions are not restored after SDF therapy, biannual reapplication shows increased caries arrest rate versus a single application.

Safety Margin and maximum dosage: One drop (25 *M*l) is considered adequate to treat 5 teeth, and contains 9.5 mg silver diamine fluoride. So, if we are to assume the smallest patient presented with caries in the range of 10 kg the dose would be 0.95 mg / kg child. Thus, the relative safety margin of using an entire drop of SDF on a child of 10 kg body weight would be: 380 mg/kg LD50 / 0.95 mg / kg dose = 400-fold safety margin (w).

Silver Nitrate is known to cause dark staining, when spilled on clothes, skin, tabletops, etc. and one should consider working very carefully around it [14]. Although the staining on the skin is not permanent, it can be there for quite some time and does not come off with regular soap or detergent. Furthermore, the European Union classifies silver nitrate as both corrosive © and dangerous for the environment (N). Also, the US National Fire Protection Association has classified silver nitrate as an oxidizer which can cause temporary incapacitation or any other possible residual injury [15].

Advantages [47]

- Atraumatic and minimally invasive
- Cost effective
- Easy to use
- Does not require additional equipment
- Less time consuming
- High patient acceptance
- No mixing required; available as ready to use

Disadvantages [47]

- Causes staining of the carious tooth surface compromising aesthetics
- May not always be successful in arresting the lesion. Relies on the cleansing action of the patient
- Difficult in measuring the success or the outcome
- Might be slow in preventing pulp involvement in case of severe carious lesions
- Metallic taste

Silver diamine fluoride is a safe, effective treatment for dental caries across the age spectrum. It is a minimally invasive, low-cost, and simple method that can be readily acceptable by fearful and anxious young children. For children who cannot be prescribed for traditional restorative treatment, it serves to be a useful immediate treatment for children accompanied by dental decay. It is effective for caries arrest and prevention of new lesions on the teeth where it is applied, and it is a minimal intervention treatment that is safe and affordable. The purpose of arresting caries treatment is to halt or slow down caries progression in order to minimize the discomfort and potential pulpal damage.

The characteristic trademark of SDF is a visible dark staining that is a sign of arrest of caries on treated dentin lesions. The main adverse events associated with SDF applications are pulpal irritation, dental staining, and oral soft tissue irritation. It has been reported as innocuous to the dental pulp. Several studies have highlighted the black dental stains that appear after SDF application as one of its disadvantages. An *in vitro* study demonstrated that tooth discoloration could be reduced by the incorporation of potassium iodide to SDF during application. This dark discoloration is permanent unless restored. Although staining on anterior teeth was perceived as undesirable, most parents preferred this option to avoid the use of advanced behavioral guidance techniques such as sedation or general anesthesia to deliver traditional restorative care. It was also found that about one-third of parents found SDF treatment unacceptable under any circumstance due to esthetic concerns. To identify those patients, a thorough informed consent, preferably with photographs that show typical staining, is imperative. To improve esthetics, once the disease is controlled and patient's circumstances allow, treated and now-arrested cavitated caries lesions can be restored.

Fig 4: IMG 03 – Staining due to SDF

Dos of Silver Diamine Fluoride

- Read the manufacturer's instruction manual carefully.
- Explain the risks of discoloration to tooth structure before application. If a restoration is stained, the stain should polish off, but staining around margins may remain.
- Have your patients wear protective eyewear and cover exposed clothing in the head and neck area.
- If silver diamine fluoride comes in contact with skin, try to absorb as much as possible with a piece of gauze and blot the area of any excess material. After that, wash the area thoroughly with soap and water, 3% peroxide, or an iodine tincture

Don'ts of Silver Diamine Fluoride

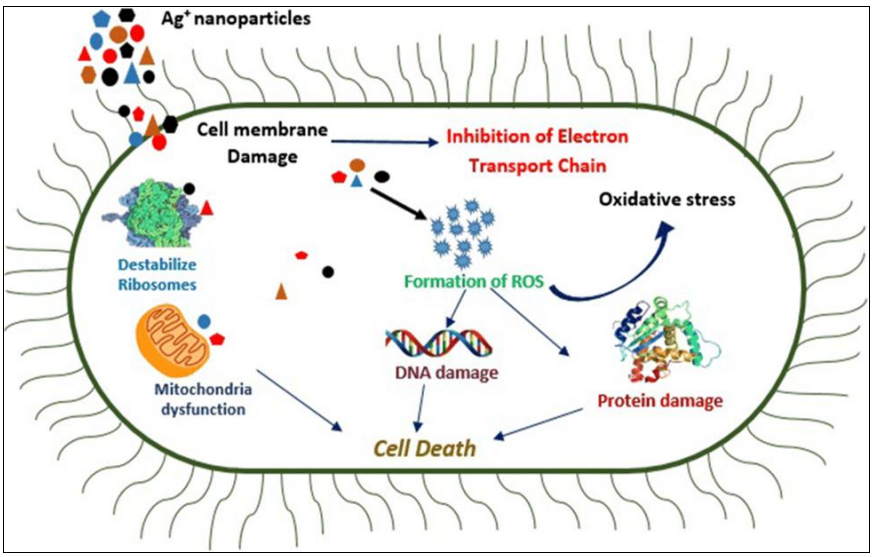
- Do not take more than 1 drop for treating up to 5 units.
- In case of any staining on the mucosa, do not wipe it; wiping can spread it and result in a larger stain.
- Don't dispose the SDF stained microbrush on the counter/tabletops as it can stain them.

Limitations and additional considerations for SDF

Safety and pulpal interactions have been thoroughly studied and it has shown that SDF has an excellent safety record [52, 53] However, a recent abstract submitted at the International

Association for Dental Research meeting exhibited cytotoxicity to fibroblasts through the use of SDF *in vitro* 9 weeks after it was applied to hydroxyapatite discs. This study reported an increase in the death of pulpal cells when the remaining dentinal thickness between the applied SDF and pulp was reduced [54].

Now there are two available forms of silver particles: ionic silver and silver nanoparticles. Till date ionic silver is most commonly used in commercially available SDF, whereas silver nanoparticles have only recently been developed [55]. This recent discovery may be as effective as SDF without the unaesthetic appearance of any dark stains on the carious tooth surfaces. It has been found that the antimicrobial efficacy and transparency of the nanoparticles increase as their size decreases. These extremely small particles, roughly around 10-nm pass into the bacterial matrix and disrupt the vitality of the bacterial cells, especially for the gram-negative bacteria. However, additional clinical studies are to be required for determining the adequate concentration of silver nanoparticles and whether they produce any discoloration post application.



Courtesy: Endophyte-mediated synthesis of silver nanoparticles and their biological applications - Scientific Figure on Research Gate

Fig 5: IMG 04 – Mechanism of action of Ag+ nanoparticles

SDF application in older adult patients: The older patient population are at a greater risk of caries than never before.[56] It is mainly due to their existing medical conditions, physical fragility, psychological beliefs and constraint financial situation. Apart from that, systemic conditions, such as diabetes, xerostomia, Alzheimer's etc., further dispose as a barrier for a better oral health. When compared to younger patients, the older adults are also presented with more tooth surfaces that are likely to be decayed.

It has been noted that the disease pattern in the older population is different from that of the younger population. A vast majority of dental problems in this population is recurrent disease associated with failed restorations, especially at the gingival margin.[57] New lesions continue to progress despite the usage of glass ionomer cements or composites in the xerostomic patients.

In the current scenario, research proclaim that an annual application of SDF is a better treatment modality than fluoride varnish or chlorhexidine varnish applied four times a year, in arresting root caries in older adult patients [58]. An improvement in the efficacy of the overall treatment is greatly enhanced with frequent application [59, 60] and with higher concentration of SDF. [60, 61]

Amid the older population, the primary indictions for topical SDF treatment are as follows:

- Diificult-to-treat lesions, as in furcations and crown margins.
- As a preventive measure in vulnerable surfaces such as gingival margins of compromised restorations, root recession.
- Patients with extreme risk of caries (e.g., xerostomic patients or patients on hyposalivary medications)
- Patients who are unable to cooperate (e.g., Alzheimer's, Parkinson's, dementia)
- Individuals with lack of insurance or limited finance.

Comparison to other topical agents: Upon comparison, it was seen that an annual application of SDF revealed significantly higher prevention results as compared to quarterly application of 5% sodium fluoride varnish [32]. A similar result was obtained from a large number of studies conducted on older adult patients [58]. Hence, we can say that an annual application of SDF per year can help arrest carious lesions and as effectively as biannual or quarterly application of sodium fluoride varnish per year.

Comparison to sealants: SDF application as a sealant for preventing lesions on newly erupted first molars is debatable. In one study, it was observed that the prevention rate of SDF was higher than that of the control group by resin sealants [62]. However, another study revealed a greater arrest of the lesions when treated with glass-ionomer sealants than SDF [63]. So, a direct conclusion cannot be made but SDF-mediated treatment most likely depends on the number of applications annually and maintenance of oral hygiene [64].

Good patient management is still profoundly relevant to the very young and otherwise old and challenged patients, though this one-minute intervention is more tolerable than other options. In the future, fluoride varnish might be replaced by Silver Diamine Fluoride for the prevention of caries in patients who have active carious lesions. This is a powerful new tool in the fight against dental caries particularly suited for those who suffer the most from this disease.

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