

Silver Diamine Fluoride: Journey from Silver bullet to Magic Bullet

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Abstract: Development of the latest advanced instruments, materials, and techniques has enabled the clinicians, a transition from G.V. Black's "Extension for prevention" to the "Prevention of extension" approach in caries management. Although silver diamine fluoride (SDF), is not new but has recently gained tremendous popularity among clinicians globally due to its effectiveness in arresting the progression of carious lesions without the need for any aerosol procedure during this COVID 19 pandemic time. Silver diamine fluoride can be used topically directly on carious lesions which have been shown to arrest remaining decay, prevent dental caries, remineralize and harden leathery dentin leading to the dark color change. Since the management of dental caries with SDF is non-invasive and much comfortably performed, it can be a favorable means to treat dental caries in children, adults, and particularly in special health-care needs.

Keywords: Silver Diamine Fluoride, Silver bullet, caries arrest, Remineralizing agent, Noninvasive caries management

1. Introduction

Miles Markley, one of the pioneers in preventive dentistry, summarized the idea behind the treatment of dental caries as "the loss of even a part of a human tooth should be considered as a serious injury, and that should be the dentist's goal today to preserve healthy, natural tooth structure" [1]. Trends in dental caries in Indian children for the past 25 years (1992-2016) shows a pooled prevalence rate ranging from 50.8% to 62.4% till 15 years of age group children [2]. The mean prevalence of dental caries is almost similar at 5 years and 12 years is 49% while it shows a steady increase at 15 years (60%) [3]. The most challenging part is to provide preventive and therapeutic treatment to dental caries in children below 15 years of age which make up 30.76% of India's population [4]. Therefore the need of the hour is to find a solution that is quick, inexpensive, and equally effective in caries arrest and prevention. "Silver Diamine Fluoride" topical solution is the answer to the above question containing silver and fluoride with ammonia. SDF helps in decreasing the CFU (Colony Forming Units) counts of *S. mutans* and *Actinomyces naeslundii* which arrest and prevent the carious lesion [5]. SDF also increases the mineral content of dental hard tissues by enhancing the absorption of calcium, which significantly increases the surface microhardness of carious lesions [6,7,8].

2. Historical Perspective

The first reported use of silver in medicine was to store water in the silver vessel due to its antimicrobial property back in 1000 BC [9]. In dentistry silver nitrate (silver

amalgam and nitric acid) was used to arrest caries back in 1891 [10]. According to Stebbins caries reduction with silver nitrate was due to antibacterial action and the deposition of a "black crust," producing a sclerotic protective layer of secondary dentin. Silver nitrate was also used as a treatment for hypersensitivity. Howe in 1917 used ammoniacal silver nitrate solution popularly known as Howe's solution on carious lesions that resulted in a black layer of sclerotic dentin, which appeared to arrest the development of future carious lesions [11]. But doubts on its clinical efficacy and possible adverse effects on the pulp limited its use for nearly one half of a century. Western Australia introduced AgF as a part of the minimal intervention program in school dental services [12]. Study on Silver diamine fluoride was pioneered by Nishino and Yamaga at Osaka University in Japan in 1969 by combining the potent antimicrobial properties of silver with the benefits of a high dose of fluoride [13]. This formulation also resulted in a precipitate that occluded dentinal tubules and reduced hypersensitivity. In 1970 "silver diamine fluoride" got approval by the Central Pharmaceutical Council of the Ministry of Health and Welfare of Japan as a cariostatic agent and was marketed as Saforide (Toyo Seiyaku Kasei Co. Ltd, Osaka, Japan) [14]. In 2014, the US Food and Drug Administration approved SDF as an agent for dentin desensitization in adults and, in 2015, the first commercial product became available in the United States as "Advantage Arrest". Advantage Arrest (Elevate Oral Care, LLC, West Palm Beach, FL) is a 38% SDF solution [15]. A new code, D1354, for "interim caries arresting medication application" was approved by the Code on Dental Procedures and Nomenclature (CDT) Code Maintenance Commission for 2016 [16]. In 2017, the

American Academy of Pediatric Dentistry published a Guideline for the “Use of Silver Diamine Fluoride for Dental Caries Management in children and adolescents, including those with special health care needs” [17]. In 2016 World Health Organization (WHO) published a report on Public Health Interventions against “Early Childhood Caries” and concluded that silver diamine fluoride can arrest dentin caries in primary teeth and prevent recurrence after treatment [18].

Misinterpreted or misspelled nomenclature as silver diamine fluoride:

The neutral silver fluoride compound by itself is unstable. To make it stable neutral silver fluoride is dissolved in ammonia to form stable diammine complex. So, the appropriate terminology is silver diammine fluoride containing two ammine groups (NH₃), not two amine

groups (NH₂). Although the appropriate term is silver diammine fluoride, most of the time it is misspelled as silver diamine fluoride which has been accepted by both the scientific and promotion platforms [19].

Composition of SDF:

SDF solutions are basically composed of ammonia, silver, and fluoride. The fluoride content in SDF solutions varies depending on the brands and the manufacturers. The most commonly used concentration of SDF is 38% containing 44,800 ppm F and 255,000 ppm Ag. As available in the United States, SDF is a colorless topical agent (38% w/v Ag(NH₃)₂F, 30% w/w) comprised of 24.4–28.8% (w/v) silver and 5.0–5.9% fluoride, at pH 10, and marketed as “Advantage Arrest” by Elevate Oral Care, LLC, West Palm Beach, Florida [20]. Other available concentrations of SDF solutions are mentioned below (Table 1) [21].

Table 1: Commercially available different brands of SDF solution [17,22,23]

Serial No.	Product brand	Manufacturer	Country	Ingredients	Package	SDF(%)
1	Cariostatic	Inodon Laboratio	Brazil	SDF	5ml dropper bottle	10
2	Cariestop	Biodinamica	Brazil	Fluoridic acid, silver nitrate, ammonia	5ml or 10 ml dropper bottle	12 and 30
3	Bioride	Dentsply	Brazil	SDF	5ml dropperbottle	30
4	Riva Star	SDI Dental Ltd	Australia	Unit1: Silver, fluoride, ammonia Unit 2: Potassium, iodine, methacrylate s	5ml dropper bottle	30-35
5	e-SDF	Kids-e-dental, Mumbai	India	SDF	5ml dropperbottle	38
6	FAGamin	Tedequim SRL	Argentina	SDF	5ml dropper bottle	38
7	Fluoroplat	NAFlaboratorio	Argentina	SDF	5ml dropper bottle	38
8	Saforide	Toyo Seiyaku Kasei	Japan	SDF	5ml dropper bottle	38
9	Advantage Arrest	Elevate Oral Care	United States	SDF	8ml dropperbottle	38

Indications of SDF [24]:

SDF is indicated in the patients:

- Who are at high caries risk and have active cavitated carious lesions in anterior or posterior teeth
- Cavitated carious lesions presenting with behavioural or medical management challenges
- With multiple cavitated carious lesions which warrant several treatment visits
- With dental carious lesions that are difficult to treat
- Without access to or with difficulty accessing dental care

Contraindications of SDF [20]:

- SDF is contraindicated in the following situations:
- Individuals with known silver allergy
- Individuals with oral soft tissue ulcerations, especially that can come in contact during application of SDF
- Active cavitated caries lesions with pulpal involvement
- If parents/guardians do not consent for using SDF, due to the concern of discoloration.

Selection of Teeth for the Application of SDF [24]:

- No clinical signs of pulpal inflammation or spontaneous pain.
- Cavitated caries lesion not approaching the pulp. Radiographs should be taken to assess the depth of caries lesions and proximity to pulp.
- Cavitated caries lesions on any surface accessible with a brush for applying SDF. (Orthodontic separators help to gain access to proximal lesions)

- Prior to restoration placement as apart of caries control therapy.

Disadvantages [8, 25]

- Formation of an insoluble protective layer of Silver phosphate is responsible for blackish discoloration of the lesion after SDF application
- Metallic taste
- Oral and pulp tissue irritation
- Can stain gingiva, oral mucosa, skin, clothes

Methods to prevent discoloration due to SDF:

- Incorporation of potassium iodide to SDF during application (contraindicated in pregnant and lactating mother due to chances of development of thyroid abnormality in the child) [26]
- Glutathione biomolecule also reported reducing discoloration due to SDF particularly on enamel and to a minor degree on dentin [27].
- Nano-silver fluoride is reported to be as effective as SDF in arresting caries without causing staining [28].

Parental and patient acceptance:

- Crystal et al. in 2017 conducted a study regarding the acceptance of dental staining associated with SDF treatment among parents of young children in the New York City metropolitan area. In that study, 30% of parents accepted staining in anterior teeth due to SDF and 68% in posterior teeth. 60% of Parents accepted anterior

teeth staining when the alternative was dental treatment under general analgesia [29].

- The survey in Hong Kong by Duangthip et al. in 2018 showed more acceptance of posterior teeth staining rather than anterior teeth staining and overall acceptance to be 61–71% [30].

Clinical protocol prior to application [24]:

Prior to the SDF application, informed consent should be obtained from parents/caregivers and patients regarding staining of treated lesions, potential staining of skin and clothes, and need for reapplication.

Clinical application of silver diamine fluoride (AAPD chairside guidelines on SDF, 2017) [24]

- STEP 1: Removal of gross debris from cavitation.
- STEP 2: Carious dentin excavation prior to the SDF application is not necessary unless there is a question of aesthetics.
- STEP 3: A protective coating of petroleum jelly is applied to the lips and skin prior to SDF application to prevent a temporary henna-appearing tattoo formation in soft tissues. Caution should be taken not to apply to the carious lesion.
- STEP 4: Isolation is done with cotton rolls or other isolation
- STEP 5: Caution should be taken when applying SDF on primary teeth adjacent to permanent anterior teeth that may have non-cavitated (white spot) lesions to avoid unnecessary staining.
- STEP 6: One drop of SDF should be used for the entire appointment.
- STEP 7: The lesion is dried with a gentle flow of compressed air.
- STEP 8: Bend a micro sponge brush. Dip the brush into SDF and dab on the side of the plastic dappen dish to remove excess liquid before application.

- STEP 9: Apply SDF directly to only the affected tooth surface.
- STEP 10: Excess SDF is removed with gauze, cotton roll, or cotton pellet to minimize systemic absorption.
- STEP 11: The application time should be at least one minute if possible with a gentle flow of compressed air until medicament is dry. Three minutes of isolation of the treated area is needed.
- STEP 12: 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 [24]:

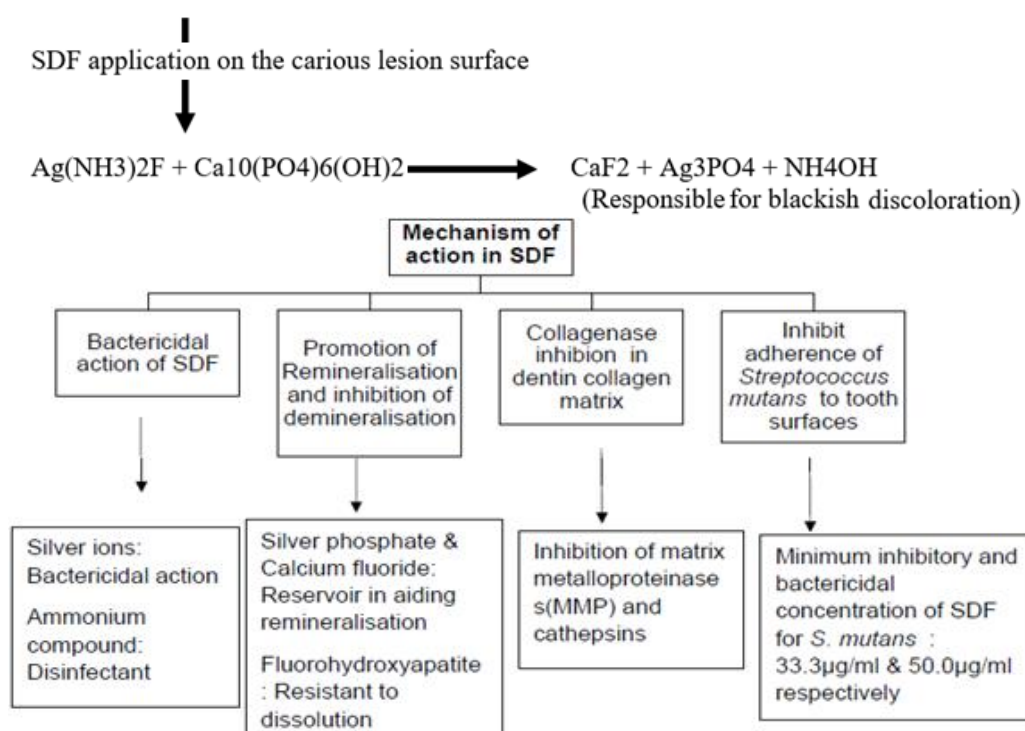
- Follow-up should be done after 2-4 weeks of initial treatment to check the arrest of the treated carious lesions.
- If the treated lesions do not show hardness and dark color, the reapplication of SDF is indicated.
- Restoration can be done after treatment with SDF.
- If lesions are not restored after SDF therapy, bi-annual reapplication is advised.

Mechanism of Action of SDF:

When SDF is applied to the carious lesion surface, it reacts with hydroxyapatite to form silver phosphate and calcium fluoride.

Mainly three actions have been proposed:

- 1) bactericidal action of SDF on cariogenic bacteria such as *Streptococcus mutans* [5,7]
- 2) promotion of remineralization and inhibition of demineralization of enamel and dentin [7]
- 3) reduction of dentine collagen matrix destruction through collagenase inhibition [5] Suzuki et al. and Tsutsumi et al. proposed the fourth mechanism of action of SDF as inhibition of adherence of *Streptococcus mutans* to tooth surface [31,32]



Histological study of SDF-treated teeth [33]:

- SDF treated tooth after sectioning and study under the light microscope showed black brown stain coating suggesting of silver deposition extending 700µm towards the pulp.
- These silver deposition present in the form of elongated striations following the orientation of dentinal tubules.
- Under Synchrotron X-ray micro-CT, silver deposition appeared as bundles of microwires of 50-2,100µm in length and 2.5-7.0µm in diameter.
- From Scanning electron microscope these structures were confirmed as “Silver microwires” composed of silver and chlorine.
- These microwires apart from acting as a reservoir of silver and preventing fluid flow from dentinal tubules also increase the hardness of treated carious lesions by densification of soft organic matrix and distribution of forces through the microwires.

Effectiveness of different concentrations of SDF:

- Fung et al. in 2018 studied the effect of 12% and 38% concentrations of SDF in annual and semiannual frequency in the carious lesion in kindergartens and found that 38% SDF had 18-20% more increase in caries arrest as compared to 12% SDF. 38% SDF in semiannual application showed maximum 75.7% caries arrest rate [34].
- Yee et al. in 2009 compared single application of 38% SDF with and without reducing agent with 12% SDF alone in primary and permanent teeth and found that mean number of arrested caries was more with 38% SDF with no significant difference of with or without reducing agent [35].

Effectiveness of 38% SDF versus 5% sodium fluoride varnish application:

Chu et al. in 2002 compared the effect of a single application of 38% SDF with and without caries excavation and a single application of 5% sodium fluoride with and without caries excavation in the carious lesion in primary teeth. The result showed mean numbers of arrested carious tooth surfaces highest with 38% SDF without caries excavation [7].

Effectiveness of 38% SDF versus Glass ionomer cement (GIC) restoration:

- Zhi et al. in 2012 compared the percentage of the arrest of dentin caries in 38% SDF annual and semi-annual application with Glass ionomer restoration annually. The maximum percentage of dentin caries arrest was seen in 38% SDF semiannual application followed by 38% SDF annually and GIC restoration [36].
- Santos et al. in 2012 compared 30% SDF and Glass ionomer restoration to evaluate the percentage of the arrest of dentine caries. 30% SDF showed more caries arrest in comparison to GIC [37].

Effects of SDF on bonding:

- Quock et al. in 2012 concluded from their study that SDF had no effect on composite bonding to noncarious dentin [38].

- Knight et al. in 2006 showed that rinsing after SDF application avoided 50% decrease in bond strength for GIC [39].
- Yamaga et al. in 1993 increase in dentin bonding strength to GIC after using SDF [40].
- Soeno et al. in 2001 showed that SDF decreased dentin bonding strength of resin-based crown cement [41].

SDF in Caries Arrest of Primary Dentition:

- Chibinski et al. in 2017 reported that caries arrest at 12 months with SDF application was 66% higher than any other active materials in primary teeth [42].
- Fung et al., Duangthip et al., Zhi et al. from their studies found that caries arrest is much higher in anterior teeth than posterior teeth with the application of SDF [31,34,36].

SDF in Caries Prevention of Primary Dentition:

Llodra et al. in 2005 compared 38% SDF with regular Sodium fluoride application and found that the mean number of new decayed surfaces in 38% SDF and sodium fluoride were 0.29 and 1.43 respectively. Prevention of caries in primary dentition is more with 38% SDF in comparison to sodium fluoride application [43].

SDF in Caries Prevention and arrest of 1st Permanent molars:

- Braga et al. in 2009 studied caries arrest in 10% SDF group, GIC sealant group and, tooth brushing group. SDF was found to be more effective than tooth brushing and GIC at 3 months and 6 months [44].
- Liu et al. in 2012 studied caries prevention in permanent 1st molars using 38% SDF, resin sealant, semiannual application of 5% NaF varnish, and placebo. Progression of caries in SDF group, sealant group, varnish group, and placebo group are 2.2%, 1.6%, 2.4%, 4.6% respectively [45].
- Monse et al. in 2012 compared a single application of 38% SDF with atraumatic restorative treatment sealant in the prevention of dentinal caries. Found that ART sealant is more effective than a single application of SDF [46].
- According to MacLean J., caries lesion can be restored after SDF application with resin-modified glass ionomer or composites is termed as “SMART” [47].

SDF in caries arrest and prevention in the elderly

Hendre et al. in 2017 studied caries arrest and prevention in older adults using 38% SDF and found that preventive fraction of 24% in 24 months study and 71% over 36 months study on root caries in comparison to placebo [48].

Analysis of different studies till date revealed that semiannual application of 38% SDF alone or SDF applied as a linear beneath restorations/sealants could be a better cariostatic agent in the prevention, arrest, and management of dental caries in both primary and permanent teeth and as well in root caries when compared to 5% NaF varnish, GIC restoration, and atraumatic restorative treatment.

Toxicity and safety levels [49]:

- The average LD50(Lethal dose) of SDF is 380 mg/kg body weight. One drop is sufficient to treat 5 teeth and contains 9.5 mg silver diamine fluoride.
- Suppose a small child with 10 kg weight having caries, received 1 drop of SDF then the safety fold margin is around 400. So, the recommendation is to limit as 1 drop of SDF per 10 kg per treatment visit, with weekly intervals at most.
- According to the U.S. Environmental Protection Agency, a total lifetime silver uptake of 1g is needed for silver poisoning, corresponding to nearly 400 SDF applications.

Therefore SDF is highly safe to use topically.

3. Scope for future research

Points which need to be studied further in the future are:

- 1) Frequency and intensity of SDF, that can be used in conjunction with adjunctive preventive agents
- 2) Timing of application and follow up duration with and without the use of restorations
- 3) The longevity of arrest and prevention of caries in SDF treated tooth
- 4) Interaction of SDF at the genetic level of the oral microbiome

4. Conclusion

In today's scenario, available scientific data on SDF, no doubt proves it to be the best possible way to arrest and prevent dental caries in individuals at the office as well as at the community level. Needless to emphasize that into the present "COVID 19 pandemic" situation where generating aerosol is a big hazard, SDF can be a game-changer. So, SDF aptly deserves to be termed as "Magic bullet" in the management of dental caries.

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