Silver Diamine Fluoride: A Magic Stain- A Review

Tharani. T[1], Twinkle Chawla[2], Lakshmi Prasadh[3], Rashika Singhania[4], Sakshi Shah[5]

Post Graduate Student[1], Dept. of Pediatric & Preventive Dentistry, Manav Rachna Dental College, Faridabad, Haryana

Post Graduate Student[2], Dept.t of Pediatric & Preventive Dentistry, Manav Rachna Dental College, Faridabad, Haryana

Post Graduate Student[3], Dept.t of Pediatric & Preventive Dentistry, Manav Rachna Dental College, Faridabad, Haryana

Post Graduate Student[4], Dept. of Pediatric & Preventive Dentistry, Manav Rachna Dental College, Faridabad, Haryana

Post Graduate Student[5], Dept. of Pediatric & Preventive Dentistry, Manav Rachna Dental College, Faridabad, Haryana

Access this article online

Website: www.healtalk.in

Quick Response Code:

Abstract :

The use of a topical fluoride solution, specifically silver diamine fluoride (SDF), in dental treatment is gaining popularity. SDF has been utilized as a caries arresting and anti-hypersensitivity agent in various Asian countries, including Japan and China. The Food and Drug Administration recently approved it.In the United States, it is approved by the Food and Drug Administration as a fluoride to treat hypersensitive teeth. Topical use of SDF is a noninvasive, rapid, and easy treatment. Laboratory investigations and clinical trials have shown that SDF is more effective than other fluoride treatments in halting caries development. According to one assessment, SDF is a safe, effective, efficient, and equitable caries control agent with potentially broad applicability in dentistry and may meet certain criteria. Because SDF management of dental caries is noninvasive and much more comfortable, it can be a beneficial way to treat dental caries in youngsters. Based on the known literature, the current study provides insight into the use of SDF in pediatric dentistry and its clinical value.

Keywords: Silver Diamine Fluoride, Caries Arrest, Fluorides, Non- invasive

Introduction

Early childhood caries (ECC) is one of the conditions that affect deciduous teeth most often. Despite continuous study into the disease's origins and preventative treatments, ECC continues to have a negative influence on young children's health as well as social and economic implications.[1]

Untreated ECC has additional effects, including an increased risk of caries, loss of erupting teeth, pain, weight loss, low self-esteem, missed school days, expensive emergency care, a constrained course of therapy, and jaw bone development. Young children are at risk for developing ECC due to several risk factors, including malnutrition, low socioeconomic status, prolonged bottle feeding, frequent snacking, an iron and vitamin D deficiency, and untreated ECC has these additional effects.[2,3]

Two of the most significant public health issues impacting children in developing nations today are untreated carious lesions and a lack of dental services. Traditional mending techniques need the child's cooperation for a successful outcome and are highly time-consuming and difficult. Uncooperative kids are not the finest options in the same situation. Given the intricacy of the issue and the surrounding circumstances, a remarkable anti-cariogenic treatment has been developed, and it has shown to be advantageous for both pediatric and general dentists.[1,4]

How to cite this article: T Tharani et al.: Silver Diamine Fluoride: A Magic Stain-A Review, *HTAJOCD 2023;July-Aug(6):27-34*

A number of fluoride-based prophylactic methods and remineralizing therapies work to reduce dental cavities in children. One of these caries-arresting methods that has gained a lot of attention recently is topical Silver Diamine Fluoride (SDF) of attention from dentists all over the world since it is non-invasive, inexpensive, and simple to use while successfully halting and preventing dental caries.[3]

History[5-8]

Around 1000 B.C., silver was first used as medicine by storing water in silver pots because of its antibacterial qualities.

1891 - "Stebbins noticed that the antibacterial activity of silver nitrate was responsible for the caries decrease, and that a "black crust" developed as a protective layer of secondary dentin, lowering dentin hypersensitivity.

1917 - Howe employed ammoniacal silver nitrate, sometimes referred to as "Howe's solutions," to treat a caries lesion.

Japan's Osaka University's Nishiino and Yamaga invented silver diamine fluoride in 1969 by fusing the antibacterial capabilities of silver with the advantages of high fluoride levels.

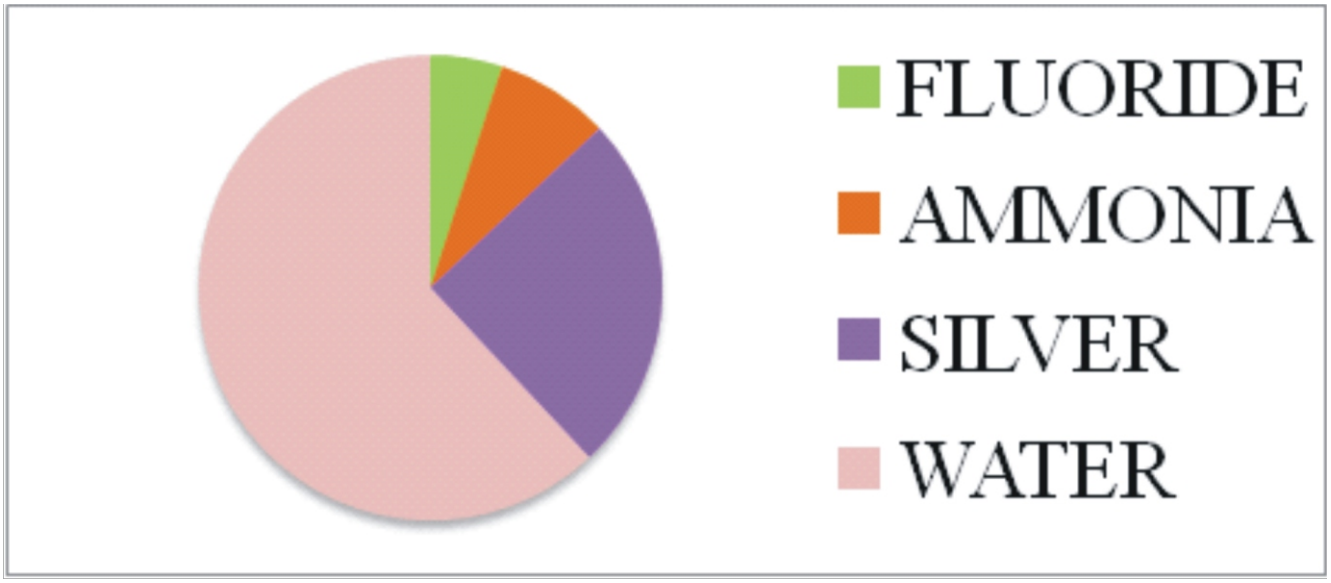
'Silver diamine fluoride' was approved as a cariostatic agent by the Central Pharmaceutical Council of the Japanese Ministry of Health and Welfare in 1970, and Saforide (Toyo Seiyaku Kasei Co. Ltd., Osaka, Japan) was made commercially available to dentists.

A new code D1354 for "interim caries arresting medicament application" was authorised by the Dental Procedures and Nomenclature (CDT) Code Maintenance Commission in 2016.

The American Academy of Paediatric Dentistry published a guideline for the "Use of Silver Diamine Fluoride" in 2017.

Composition of Silver Diamine Fluoride

Components	w/v%	Properties
Silver	24-27%	Antimicrobial
Ammonia	7.5-11%	Stabilizes High Concentration of Solution
Fluoride	5-6% (approx 44,800)	Antimicrobial And Reminerlization
Deionized Water	<62.5%	



SDF Vs Silver Fluoride

Silver fluoride (SnF2) is a colorless solution containing silver and fluoride ions. It is strongly alkaline (pH = 11), necessitating a two-stage application.

SnF2 is used as a reducing agent in this method. SDF has been shown to be less reactive and can be kept at a steady concentration. SDF is less alkaline (pH = 8-9) than AgF and does not require a reducing agent.[6]

Despite being far more soluble in water than the other silver halides, SnF2 produces colorless cubic crystals. Ammonia and SnF2 combine to create SDF. The ammonia ions combine with the silver ions to form a complex ion known as the diamine-silver ion. The formation of these diamine-silver ions is a reversible and highly stable process.[7-9]

While AgF is difficult to obtain, SDF is commonly available as a 38% solution in a commercial preparation and is known in Japan as Saforide (Toyo Seiyaku Kasei Ltd, Osaka, Japan). Saforide contains 380 mg water-soluble SDF in 1 mL of colorless aqueous solution, or approximately 44,800 ppm fluoride ions. In South America, SDF is commercially available as Fluoroplat (LaboratoriosNaf, Buenos Aires, Argentina) and Safluoride di Walter in 10% solution (Polidental, Rio de Janeiro, Brazil). In Australia, a 38% SDF solution is also available (Creighton Pharmaceutical, Sydney, Australia). In India, it is sold under the brand name FAgamin in a concentration of 38%.[10]

Properties

- A colorless aqueous solution of silver ions and fluoride ions.
- It is highly alkaline (pH = 11), necessitating a two-stage application technique involving SnF2 as a reducing agent.
- For many years, many countries, notably China and Japan, have used silver diamine fluoride, a chemical that is said to be more stable and can be kept at a constant concentration, to prevent dental caries.
- SDF is less alkaline (pH = 8-9) than AgF.
- Does not require a reducing agent.[11]

Mechanism of Action

Silver has been postulated to have multiple mechanisms of action. Silver interacts with protein sulfhydryl groups as well as deoxyribonucleic acid (DNA), affecting hydrogen bonding and suppressing respiratory activities, DNA unwinding, cell-wall synthesis and cell division, according to research.[12] These interactions have a large impact on bacterial death and the production of biofilms. The interaction of silver with thiol groups is proposed as the central mechanism underlying these various mechanisms:

$$A/N\text{-}SH + AgX \rightarrow A/N\text{-}S\text{-}Ag + HX$$

Where SH stands for a thiol group, Ag for silver, and X for an anion (in this case, diamine fluoride) and A/N for amino (A) or nucleic (N) acids, respectively. This interaction reveals how silver-containing chemicals may interact with bacteria to mediate caries arrest through bacterial death and reduce caries development through suppression of biofilm formation.[12]

Three potential modes of action for SDF on caries were described by Shimizu and Kawagoe in 1976.

1. The first mechanism could be dentinal tubule obturation. Gottlieb stated that blocking the organic invasion pathway would stop caries from occurring. Dentinal tubules are the primary invasion route for cavities in the dentin. Shimizu claims that dentin treated with SDF increased in electric resistance and reduced in dye permeability. He repeatedly confirmed that the dentinal tubules contained silver and its compounds. Therefore, the dentinal tubules may be inhibited against microbial invasion and acid diffusion. Even if bacteria enter dentinal tubules, silver's oligodynamic activity will prevent them from growing. The peritubular zone, the portion of dentin that is most readily demineralized, can be coated with obturating materials (silver particles), which minimises the surface area of dentin that can be attacked by caries. These traits must help promote resistance to recurrent caries when combined with dentinal tubule obturation. According to a recent study by Mei et al. (2013), employing 38% SDF prevented collagen from degrading and decreased demineralization in demineralized dentin.[13]
2. The cariostatic effect of the results of the interaction between SDF and tooth mineral components might be the second mechanism.Selvig[35] demonstrated that fluoride treatment enhanced the resistance of the peri- and inter-tubular dentin to acid decalcification, hence slowing acid penetration into deeper layers of the dentin. Shimooka stated that F ion of SDF applied to dentin in vivo Conditions reached a depth of 50-100. SDF (Ag(NH3) 2 F) has been shown to react with the tooth mineral hydroxyapatite (HA)(Ca10(PO4)6 (OH)2) to release calcium fluoride (CaF2) and silver phosphate (Ag3PO4), which are responsible for the prevention and hardening of dental caries.[13,14]

A simple chemical process is depicted below.

$Ca10(PO4)6(OH)2 + Ag(NH3)2 \rightleftharpoons CaF2 + Ag3PO4 + NH4OH$

$CaF2 \rightleftharpoons Ca^{++} + 2F^-$

$Ca10(PO4)6(OH)2 + 2F^- \rightleftharpoons Ca10(PO4)6F2 + 2OH^-$

The Ag3 PO4 that forms on the tooth surface is insoluble. The CaF2 generated serves as a fluoride reservoir for the synthesis of fluorapatite [Ca10(PO4) 6 F2], which is more resistant to acid attack than HA [Ca10(PO4) 6 (OH)2].Fluorapatite is so stable that it is exceptionally resistant to acid and chelating agent decalcification. Furthermore, it is known that F promotes calcification, as well as repairs lattice imperfection and enhances HA crystallinity.[15]

3. The anti enzymatic activities of the reaction products of Ag(NH3) 2 F and organic component of the tooth could be the third mechanism. Its antibacterial characteristics are derived from the suppression of enzyme activity and dextran-induced agglutination of cariogenic Streptococcus mutans strains.[16]

Sunada et al. discovered that dentin treated with Ag(NH3) 2 OH via ionophoresis increased resistance to trypsin. They speculated that it was caused by a reaction between Ag and an organic component of dentin.

Yanagida et al. discovered that dentin protein treated with Ag(NH3) 2 F was more resistant to collagenase and trypsin. Ag and their acts The addition of Ag(NH3) 2 F to organic components of the tooth may also help to prevent caries.[17]

Suzuki et al. investigated the mechanism of action of diamine silver fluoride [Ag(NH3) 2 F] as an antiplaque agent. This drug demonstrated excellent antibacterial activity against cariogenic strains of S. mutans (minimum inhibitory concentration, 0.12 mole/ml) and totally inhibited S. mutans dextraninduced agglutination at 0.59 mole/ml and sucrase activities at 0.2 mole/ml. These effects were discovered to be the result of silver ion activity. These findings suggest that silver ion may impede S. mutans colonisation on the enamel surface, which could explain the agent's antiplaque activity.[3,17]

The binding of glucan to HA was similarly demonstrated to be hindered by fluoride solution treatment, but somewhat increased by silver solution treatment.

The treatment of HA with Ag(NH3) 2 F reduced the adsorption of salivary proteins by HA. This was caused by fluoride and silver ions. As a result, SDF has a greater capacity to inhibit S. mutans than any other fluoride solution. Furthermore, Mei et al. (2013) reported that 38% SDF prevents multi-species cariogenic biofilm formation on dentin carious lesions and slows demineralization.[18]

Suzuki et al. demonstrated that following SDF treatment, fluoride ions diffusely penetrated the enamel to about 25, whereas silver ions were primarily deposited on the surface.[19]

Silver's Zombie Effect

The main feature of biocidal metals such as copper and silver is their extended action, which progressively delivers harmful cations to bacteria. Bacteria destroyed by silver particles demonstrated biocidal activity against living microorganisms. The metal ion is not destroyed after killing the bacterium, and it kills the germs repeatedly. The deceased bacteria serve as a reservoir, allowing cations to be released continuously.[20]

Histologic Findings of Dentin on SDF Application

Silver penetration into dentinal tubules can range between 50-200 microns and 1 mm. There were no microorganisms identified in the tubules. SDF can help with tertiary dental development and reduce pulpal irritation. The lesions' edges are hypermineralized, whereas portions of intertubular dentin are hypomineralized. The absorption of silver is greatest within the lesion and decreases as we approach the edge.Silver precipitation can be found in the pellicle, rod sheaths, demeneralized rods, and dentinal tubules. Around the carious lesions, silver-enriched diffusion barriers form.[21]

Indications[3]

-Patients who are highly prone to caries
- Children who are unable to access dental care.
- No signs of pulpitis
-Active carious lesion in the root surface
-Teeth that are going to be exfoliated soon

Contraindication[4]

-Children who are allergic to silver
-Having soft tissue ulcers
-Parents who refuse treatment due to black staining
-Difficulties in isolation
-Showing signs and symptoms of irreversible pulpitis
-Showing signs of peri-apical pathology .

Clinical Application[17]

- To manage children who are highly susceptible to caries
- children rated negative according to the Frankel behavior rating scale
- To prevent caries from approaching the pulp
- Highly effective in caries control in a community-based caries control program

Advantages[19]

- Controlling pain and infection
- Cost-effective
- Simple procedure
- Non-invasive procedure

-Inhibit pit and fissure caries as SDF application in pits and fissures of first molars has prevented the progression of caries and is more effective when compared with stannous fluoride.

-Root caries inhibited by annual application of SDF

-Used in dentin hypersensitivity patients

-Disinfection of root canal

-Children with medical management issues[20]

Procedure[21]

-Patient and practitioner preparation

It is advised to get informed permission and to specifically point out predicted staining of treated lesions, possible skin and clothing staining, and the necessity for repeat application for disease management.

The practices listed below can help to improve patient safety and make good use of SDF:

General safety measures.

- To stop caries, no surgical intervention is required (such as removing diseased or damaged dentin).
- Protect the patient with a bib and glasses lined with plastic.
- Isolation using cotton rolls or other suitable means.
- Because SDF corrodes glass and metal, use a dappen dish.
- Place gloves, cotton rolls, and microbrushes into a plastic trash bag with care.

-Application[21]

Clean the oral cavity of any gross debris to improve SDF interaction with denatured

- Minimise contact with gingiva and mucous membranes to reduce the risk of discoloration or irritation; think about using cotton rolls to shield the gingival tissues around the teeth.
- Use a mild airflow from a compressed air source to dry the damaged tooth surface.

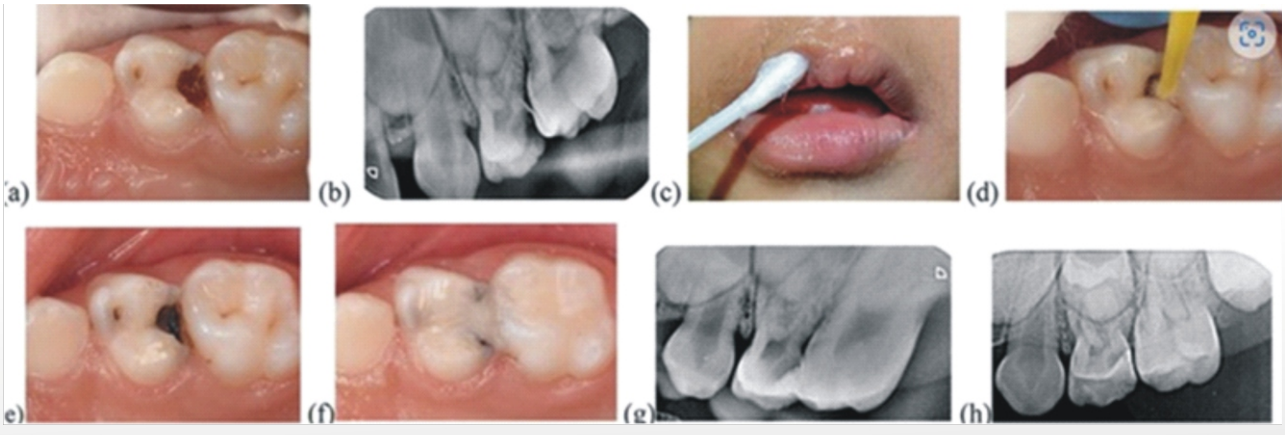
Apply SDF directly to only the damaged tooth surface using a bent micro sponge brush, dip and dab on the edge of the prepared dish to remove extra liquid, and then dry with a steady stream of compressed air for at least a minute.

- To reduce systemic absorption, remove excess SDF with gauze, a cotton roll, or cotton pellets.
- When feasible, keep the location isolated for up to three minutes.

-Application Time[19]

One minute is advised for application, followed by mild compressed air drying.

According to clinical trials, application durations might last anywhere between 10 and 3 minutes. According to a recent analysis, there is no relationship between application time and result in clinical research. Additional research is required to validate the best procedure.



Post-Operative Instructions

- After using SDF, avoid eating or drinking anything for 30 to 60 minutes.
- Follow up at 2-4 weeks after application.
- Depending on the lesion's hardness or rate of advancement, the SDF may need to be reapplied.
- Restore the carious lesions after SDF application with resin-modified glass ionomer or composite.
- If the lesions are not restored, it is advised to apply SDF every two years.[15]

Parental Acceptance

(**Marwah Almarwan, 2021)** states that "parental acceptance of SDF was higher for primary compared to permanent teeth and posterior compared to anterior teeth in both dentitions, as well."[15]

Adverse Effect of SDF

SDF is safe to use - It contains less fluoride than one application of fluoride varnish, another common method of cavity prevention.

SDF only often causes the following adverse effects:

- Gingival inflammation, however it often subsides in a few days.
- A metallic aftertaste.
- Infrequent tooth and gum discomfort [16]

Other risk factors are :

☆ Discolouration

The discoloration is among the SDF adverse effects that are most often observed. Silver phosphate (Ag3PO4), which is produced when dental caries are treated with SDF, is assumed to be the cause of its characteristic black or dark brown color. Sunlight easily causes silver phosphate to become black.

After placing the SDF, use salt to stop discoloration. Silver phosphate is not produced as a result of the salt's reaction with the remaining free silver ions.

One of the salts to avoid stains is KI, which creates silver iodide, a creamy white reaction product that, with enough application, becomes colorless. [15]

☆ Bond Strength

According to a theory, SDF weakens the binding between adhesive materials and teeth because it creates a new interface at the tooth restoration complex and obstructs dentinal tubules, which prevents adhesive agents from penetrating the tubules.[18]

Contrarily, it's interesting to note that certain products even assert an increase in binding strengths. However, the research on SDF's influence on binding strength has produced conflicting results.[20]

☆ Effect on Dentino-pulp Complex

Due to the possibility for silver ions to enter the pulp complex, it has been advised that SDF should not be utilized in carious lesions that are near the pulp.[21]

SDF exhibits potential qualities for application in deep carious lesions and as an indirect pulp-capping substance. By minimizing the quantity of tissue that needs to be removed, its capacity to stop dentine caries may also lessen the number of iatrogenic pulpal exposures.

There is presently no research on SDF's impact on pulp exposures and direct pulp capping procedures. [22]

☆ SDF Effect on the Gingiva

Gingival erythema, gingival inflammation, gingival whitening, and gingival pain have all been linked to SDF. It was reported that this was mild and just temporary (lasting less than seven days).

Additionally, there was no persistent staining of the gingiva present with this erythema.[23]

☆ SDF Effect on Mucosa & Skin

SDF's high pH might cause mucosal or skin burns after application. The burns are often little, hardly painful white lesions in the mucosa that go away on their own after 48 hours without medical attention. [24]

SDF may also leave stains on skin, clothing, and other surfaces. SDF skin staining is not painful or harmful, but it is difficult to remove and takes around seven days to go gone. However, SDF clothing stains are irreversible.[25]

Advancements in SDF

Silver-Modified Atraumatic Restorative Technique

The rationale for SMART: By physiologically sealing the tooth with caries, the remaining carious dentin's viable bacteria are deprived of their sucrose substrate and eventually die.

Therefore, the prognosis of the tooth would be considerably improved if the organisms were rendered nonviable using SDF and the staining was removed using KI before the installation of a restorative material like GIC as implanted in ART. [16]

Following SDF, placing a restoration would avoid space loss, stop the approaching fracturing of the remaining tooth structure, make it simple to remove biofilm, and do away with the requirement for advanced behavior guiding.[16]

Ammonia Free Silver Fluoride

To overcome the side effects of SDF such as inflammation of the gingiva, irritation to the mucosa, and odor of ammonia during application of SDF, water-based silver fluoride (AgF) solution has been introduced lately which has all the properties of SDF without the inclusion of ammonia. [3]

SDF With Potassium Iodide:

The remaining free silver ions in the solution would react with potassium iodide to form creamy white silver iodide crystals after SDF was applied to the tooth structure. As a result, there aren't any free silver ions left in the mouth to combine with compounds like sulphur and create black precipitates inside the teeth.[3]

Riva Star Aqua (Australia), a next-generation water-based silver fluoride solution
38% AgF

Creighton Dental CSDS – ammonia-free (Australia) at 40%.

In advanced research, SDF is now being tried as **Gel**.[25]

A novel method incorporating the application of SDF **and Light Curing** is now being investigated.[25]

Conclusion:

Children can use silver diamine fluoride since it doesn't require anaesthesia or drilling, which cuts down on anxiety and chair time **(Slayton RL, 2018).**

SDF is also efficient, affordable, and sustainable for high-risk patients of all ages.

The literature suggests additional studies to evaluate SDF's effectiveness in preventing dental caries in permanent molars and to identify the state of the arrested lesions if therapy is discontinued after 2-3 years.

References

1. **Crystal YO, Niederman R**. Evidence-Based Dentistry Update on Silver Diamine Fluoride. Dent Clin North Am. 2019 Jan;63(1):45-68. doi: 10.1016/j.cden.2018.08.011. PMID: 30447792; PMCID: PMC6500430.
2. **Singh M, Agrawal N, Ghosh J, Bhattacharya M.** Silver Diamine Fluoride: A Magic Bullet. Journal of Advanced Medical and Dental Sciences Research. 2022 Mar 1;10(3):87-91.
3. **Shah S, Bhaskar V, Venkatraghavan K, Choudhary P, Trivedi K**. Silver diamine fluoride: a review and current applications. Journal of Advanced Oral Research. 2014 Jan;5(1):25-35.
4. **Greenwall-Cohen J, Greenwall L, Barry S.** Silver diamine fluoride - an overview of the literature and current clinical techniques [Internet]. Vol. 228, British Dental Journal. 2020. p. 831–8. Available from: http://dx.doi.org/10.1038/s41415-020-1641-4
5. **Surendranath P, Krishnappa S, Srinath S**. Silver Diamine Fluoride in Preventing Caries: A Review of Current Trends. Int J Clin Pediatr Dent 2022;15(S-2):S247-S251
6. **Midentistry. Riva** Star Aqua. Dental Materials & Device Register. 2021 Nov 1;5(6):184-6.
7. **Guide C.** Silver diamine fluoride in the management of dental caries lesions. Pediatr Dent. 2017;39(6):478-9.
8. **Fung M H, Duangthip D, Wong M C, Lo E C, Chu C H.** Randomized clinical trial of 12% and 38% silver diamine fuoride treatment. J Dent Res 2018; 97: 171–178. 57.
9. **Zhi Q H, Lo E C M, Lin H C.** Randomized clinical trial on effectiveness of silver diamine fuoride and glass ionomer in arresting dentine caries in preschool children. J Dent 2012; 40: 962–967.
10. **Contreras V, Toro MJ, Elías-Boneta AR**, Encarnación-Burgos MA. Effectiveness of silver diamine fluoride in caries prevention and arrest: a systematic literature review. General dentistry. 2017 May;65(3):22.
11. **Natarajan D.** Silver Modified Atraumatic Restorative Technique: A Way Towards "SMART" Pediatric Dentistry During the COVID-19 Pandemic. Frontiers in Dentistry. 2022 Mar 17.
12. **Jain M, Jain V, Agarwal N.** A review on application of silver diamine fluoride in dentistry. Int J Oral Health Dent. 2018;4(2):58-62.
13. **Roberts A, Bradley J, Merkley S, Pachal T, Gopal JV, Sharma D**. Does potassium iodide application following silver diamine fluoride reduce staining of tooth? A systematic review. Australian Dental Journal. 2020 Jun;65(2):109-17.
14. **Rosenblatt A, Stamford TC, Niederman R.** Silver diamine fluoride: acaries "silver-fluoride bullet." J Dent Res. 2009;88(2):116-125.
15. **Korwar A, Sharma S, Logani A, Shah N.** Pulp response to high fuoride releasing glass ionomer, silver diamine fuoride, and calcium hydroxide used for indirect pulp treatment: An in-vivo comparative study. Contemp Clin Dent 2015; 6: 288.
16. **Yokoyama K, Kimura Y, Matsumoto K, et al**. Preventive effect oftooth fracture by pulsed Nd:YAG laser irradiation with diamine silver
17. **fluoride solution.** J Clin Laser Med Surg. 2001;19(6):315-318.
18. **Chu CH, Mei ML, Lo EC.** Use of fluorides in dental caries management. Gen Dent. 2010;58(1):37-43; quiz 44-45, 79-80
19. **Rossi G, Squassi A, Mandalunis P, Kaplan A.** Effect of silver diamine fuoride (SDF) on the dentin-pulp complex: ex vivo histological analysis on human primary teeth and rat molars. Acta OdontolLatinoam 2017; 30: 5–12.
20. **Conover, E., 2015.** Silver turns bacteria into deadly zombies. [online] Science.org. Available at: <https://www.science.org/content/article/silver-turns-bacteria-deadly-zombies> [Accessed 26 July 2022].
21. **Nuvvula S, Mallineni SK**. Silver diamine fluoride in pediatric dentistry. Journal of South Asian Association of Pediatric Dentistry. 2019 Jul;2(2):74.
22. **Peng JJ, Botelho MG, Matinlinna JP**. Silver compounds used in dentistry for caries management: a review. J Dent. 2012;40(7):531-541.
23. **Nishino M.** [Studies on the topical application of ammoniacal silverfluoride for the arrest of dental caries]. Osaka DaigakuShigaku Zasshi.969;14(1):1-14.
24. **Stebbins EA.** What value has argentinitras as a therapeutic agent indentistry? Int Dent J. 1891;12:661-670.
25. **Duffin S.** Back to the future: the medical management of cariesintroduction. J Calif Dent Assoc. 2012;40(11):852-858.