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NANOSILVER FLUORIDE: ULTIMATE BLESSING FOR THE CARIOUS TEETH

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ABSTRACT

Objectives: The purpose of this article is to emphasise the importance of the novel Nano Silver Fluoride against dental caries. **Data/ Source:** The searches were carried out on Medline/PubMed, Scopus, and the cross references were checked. **Paper Selection:** Original research and reviews were included. Papers, abstracts, and posters presented at conferences were not chosen. **Conclusion:** Silver nanoparticles significantly enhance the surface area available to microorganisms, thus boosting antimicrobial activity. NSF can be an ultimate and excellent way of arresting the carious lesion when administered directly to caries lesions with the aesthetic outcome by eliminating the drawbacks of discoloration with Silver Diamine Fluoride (SDF).

KEYWORDS: Nano Silver Fluoride, dental caries, Preventive dentistry, Minimally Invasive Dentistry.

ABBREVIATION

NSF - Nano Silver Fluoride
SDF- Silver Diamine Fluoride
AgNPs - Nano Silver Fluoride. Silver nanoparticles
LIDC - Low Intensity Direct Current
K2 CO3 - Potassium carbonate
FHAP or FAP - Fluorohydroxyapatite
PTS - Phosphotransferase system
PEP – Phosphoenolpyruvate
NSSF - Nano-Silver integrated Sodium Fluoride
NSF-GTE - Nano-Silver Fluoride with Green Tea Extract
PPF - Propolis fluoride
SMH - Surface microhardness
SMHR - Percentage of surface hardness recovery.

INTRODUCTION

Dental caries is an incurable but avoidable disease of the dental hard tissues that results from the oral cavity's continuous demineralization/remineralization cycle. It affects individuals of all ages. Although caries may be prevented and perhaps cured early, it is not a self-limiting illness. If not treated correctly, it may progress to the point of tooth destruction. It is defined as the localized breakdown of hard tooth tissues caused by bacteria's acidic synthesis of dietary carbohydrates. Demineralization of the carious lesion is evident on hard dental tissues even if the lesion process starts within the bacterial biofilm (dental plaque) that covers a tooth surface. It is a complicated disease that starts with microbial alterations in complex biofilms which is generally affected by component and flow rate of saliva, followed by exposure to fluoride, oral hygiene maintenance and the frequency and amount of sugar intake.[1] A dental plaque biofilm is formed on the tooth surface, gingiva, and restorative or prosthetic materials when different type of cariogenic or non-cariogenic bacteria adhere on it. Consequently, a well organise dental plaque is formed on these surfaces with complex ecosystem. This ecosystem inside the dental plaque become unbalanced due to several environmental changes such as low pH or sugar intake which will favour the development of cariogenic bacteria.[2] In the early 1900s, G.V Black discovered silver nitrate as a very effective agent for halting carious lesion formation. Additionally, he set rules for its use.[3] For more than a century, number of silver formulations have been utilized to treat various ocular, surgical, and dental diseases. At quantities less than 50 ppm, silver ions have the potential to destroy harmful organisms. It has antimicrobial properties and may be utilized in topical dressings for burn wounds, cannula or catheter linings, water decontamination, hospital cloths or gowns, and prevention of carious lesion. Miller et al. showed the intense germicidal action of silver nitrates in 1905, Howe et al. in 1917, and Klein and Knutson in 1942. Marinho et al., 2002, 2004 established fluoride's potential to prevent dental cavities.[4] A more recent silver-containing material, Silver Diamine fluoride (SDF), has been discovered to have antibacterial characteristics owing to its ability to release fluoride ions, thus assisting enamel remineralization quickly. Dentists advocate it as a helpful caries prevention treatment in many nations, including Japan, India, Australia, and the United States. It is an easy, non-invasive, and cost-effective method of avoiding caries. It outperforms fluoride varnish. Despite

its ability to prevent and treat cavities even when used yearly, it does have a few disadvantages, including tooth discoloration and a metallic taste.[3] The need for innovative materials with a solid aesthetic component has resulted in developing novel silver compounds such as Nano Silver Fluoride. Silver nanoparticles (AgNPs) are silver particles having a diameter of less than 100 nm. Silver nanoparticles significantly enhance the surface area available to microorganisms, thus boosting antimicrobial activity. Numerous theories support the antimicrobial activity of silver nanoparticles. Silver ions are employed as an antibacterial agent in a variety of consumer goods, including spraying sprays, air breathers, bowls, socks, wet wipes, air sanitizer, detergents, soap stuff, shampoos, toothpaste, and washing machines; as bone cement; and in a variety of wood treatments. These ions are used in dental composites, medical devices, and a bactericidal coating for water filters.[5]

This article will discuss the efficacy of Nano Silver Fluoride (NSF), a relatively novel material, in various clinical settings as a non-invasive treatment option.

A QUICK LOOK BACK

Stebbins et al. reported a reduction of caries after dental amalgam repair in 1891. It was believed to be caused by bacterial death and "black crusting" caused by the dental amalgam, which formed a sclerotic protective layer over the secondary dentine. Dr Percy Howe and colleagues added ammonia to silver nitrate in 1917 to create a solution of diamines of silver nitrate (Howe's solution) that was more stable and effective in containing caries lesions. It was popular in the early twentieth century, and many dentists created their formulas.[6] For almost half a century, Howe's solution has been used as a disinfectant for bacterial colonization of dental hard tissue, as a bacterial disclosing solution in preventing pulpal exposures, identifying initial white spot lesions, and revealing remaining carious portion in the dentin.[7] In 1969, Nishino M and Yamaga R combined the effects of F- and Ag+ in Japan, culminating in the approval of the first Silver Diamine Fluoride product in 1970. They addressed its benefits on preventing and arresting dental cavities in youngsters, preventing secondary caries after restorations, and desensitizing hypersensitive dentin.[7] In 1978, E A Thibodeau demonstrated the efficacy of silver ions produced using Low Intensity Direct Current (LIDC) against bacteria in selective specimen of carious dentin and the reactions of various distinct dental microorganism to silver ions produced using LIDC. It was revealed that the inhibitory effects of silver were effective in suppressing the growth of different bacterial flora of selective specimen of carious dentin and also in the pure cultures.[8] In 1973, Hyde showed the use of silver compound containing nitrate and fluoride formulation of silver, demonstrating that the fluoride formulation of silver had the ability to stop the initiation of carious lesions in proximal contact areas.[6] In 1980, Oppermarm, R. V., and Johaasen, J., R established the efficiency of metal and fluoride components in silver fluoride and copper fluoride's interference on acidic nature of the dental plaque. Moreover, it was discovered that all of the metals tested were preserved in plaque.[9] In 1983, Von Naegeli showed that a silver ion concentration of 0.0000001 percent could kill the average Spirogyra freshwater.[6] Since 2002, many clinical studies have been carried out to demonstrate the effectiveness of Silver Diamine fluoride (SDF) and compare its efficacy to that of other chemo-preventative agents. These comparative studies established SDF's effectiveness as a caries arrester. SDF was accepted by the US Food and Drug Administration in 2014 as a dentine desensitizing agent. Advanta Arrest became the first tradeable security in the United States in 2015. It contains 38% SDF.[6] Due to the inevitable staining property of silver diamine fluoride (SDF) on the tissue surface, GM Knight showed in 2006 the utilisation of Potassium iodide after applying silver diamine fluoride on teeth where he observed the production of white silver iodide.[6] The need for alternative materials has resulted in discovering of Nano Silver Fluoride (NSF). According to the United States Geological Survey, silver production was 21,300 and 21,400 tonnes in 2008 and 2009. The antimicrobial effect of silver and nitrogen have been discovered throughout time, proceeding in the widespread use of nanoparticles of silver. (10) Li et al. demonstrated in 2010 that AgNPs penetrate exterior membrane permeability, a phenomenon dubbed 'pits.' Fatema Mirzajani showed the activity of AgNPs against Gram-positive bacteria in 2011 and discovered a strong connection between AgNPs and PGN. Individual AgNPs or the Ag+ discharge interacts with the cell walls of bacteria. The Gram-positive bacterial cell wall was damaged as a consequence of AgNP treatment.[11] In 2018, Esilva et al. showed that Nano Silver Fluoride (NSF) was more efficient in treating initial carious lesions than conventional fluorides due to its capacity to remineralized the carious lesion.[11]

STEPS OF NANOSILVER FLUORIDE PREPARATION

According to Dos Santos Jr et al. in 2014, Nano Silver fluoride is a novel experimental formula involving a sequence of preparation steps in laboratory. Firstly, chitosan of 1.0g was dissolved into 200 mL of acetic acid (2 %) for distilling colloidal silver. The solution was stirred overnight and then filtered using vacuum. 60mL of Chitosan solution was stirred continuously while being immerged in the ice and then after 30 minutes 4.0mL of sodium borohydride was added to the 1L of silver nitrate (0.012 mol) solution. The mass ratio of silver nitrate and Sodium borohydride was kept at 1:6 and the ingredients were added drop by drop. As the solution transformed from uncoloured to light yellow and then crimson, the reduction reaction of Ag+ began immediately. The silver nanoparticles were spherical in form and had an average size of 3.2 1.2 nm. Lastly, to enhanced the solution's stability Sodium Fluoride was added to the completed mixture.[12]

As a result, the final composition of Nano Silver Fluoride was as follows: a) Chitosan [28,585 mg/mL]; b) Ag+ [376.5 mg/mL]; and c) Sodium fluoride [5028.3 mg/mL].

The Chemistry Department of the Federal University of Pernambuco worked with the Northeast Technology Centre in 2012 to develop Nano-silver fluoride 400, a compound composed of AgNP, chitosan, and fluoride. Several concentrations of AgNP were tested during the production process, but only the NSF at 400 ppm achieved the required stability, which was subsequently confirmed to be three years.[13]

Numerous other techniques for the production of Nano silver Fluoride have been suggested, including the following.

1. Hughoo et al. (2014) developed a weight dilution technique for generating 5% Nano Silver Fluoride. In a light-proof brown container, 0.5g of silver nanoparticle powder was mixed to 10 ml of 22,600 ppm sodium fluoride varnish and was agitated strenuously to achieve homogenous dispersion of Nano-silver particles.[13]
2. Zuhair Al-Nerabieah et al. 2020 developed a method for physiological synthesis of Nano Silver Fluoride utilizing green tea extracts. Extract of green tea was made from 1.3 g of green tea leaves and then mixing to 100 mL deionized water in conical flask. It was then heated to 80 °C for 20 minutes and cooled to room temperature. It was filtered using Whatman® filter paper grade 1. Simultaneously, Silver Nanoparticles was obtained from the extract. Extract of green tea of about 60 mL was added to the 500 mL of deionized water. It was agitated manually to obtained a uniform mixture The pH of the solution was adjusted to 10 from 6 by continuously mixing potassium carbonate (K2 CO3). 20 ml of AgNO3 aqueous solution of about 1mM was mixed in one go. Sodium fluoride was added to increase the stability as well the cariostatic property of the solution. Until required, the final solution was stored at 4°C in a dark amber container.[14] Nano Silver Fluoride is commercially available in the form of NSF 600: nano-silver fluoride, 600 parts per million (CETENE, Pernambuco, Brazil) and NSF 1500: nano-silver fluoride, 1500 parts per million (CETENE, Pernambuco, Brazil) (CETENE, Pernambuco, Brazil).[32]

MODE OF ACTION OF NANOSILVER FLUORIDE

By shrinking silver particles to nanoparticles, their efficacy is increased due to the increased relative contact area. The antibacterial activity of nano particles of silver is inversely proportional to their size. These ions are capable of producing its effect on bacterial cell structures. It gets attached to sulphur or nitrogen-containing compounds, causing permanent damage to the structural component of the cell membrane of bacteria. Thus, in turn leading to the the loss of cell contents, and ultimately causing bacterial death. Another method is that when these nanoparticles come into contact with bacteria, they have the ability to produce free radicals. These radicals can injure and penetrate the cell membrane, leading to cell death. Additionally, these ions bind with sulfhydryl groups in proteins and Nucleic acid, influencing hydrogen bonding, respiratory activity, DNA unwinding, cell wall formation, and cell division. Additionally, it also has the ability to induce the oxidative stress response, which results in bacterial cell death. Cell membranes and DNA are disturbed and changed by reactive oxygen species.[15] Chitosan serves as a stabilizing ingredient in the formulation of Nano Silver fluoride. Chitosan converts silver ions to neutral ion thus stabilizing the particles by creating a thin cladding layer on their surface.[16] It is made when chitin is deacetylated in an alkaline solution. Chitin is nature's second most abundant polymerized carbon which is obtained from crustaceans' shells, insect cuticles, and fungal cell walls. It composed of D-glucosamine units consisting of single amino group. The interaction of positively charged amino acids, NH3+, with bacteria negatively charged electrostatic surface may result in cell wall disintegration. This may result in the leakage of cell contents due to alteration the property of cell membrane. Chitosan is effective against wide range of Gram positive or negative bacteria, with an antimicrobial concentration of 100 to 100,000 mg 1-1 for gram-negative bacteria and 100 to 1,250 mg 1-1 for gram-positive bacteria.[17]

Fluoride's interaction with the mineral component of teeth leads to the production of fluorohydroxyapatite (FHAP or FAP), which is formed when OH- is replaced by F-. This results in increased hydrogen bonding, a more rigid crystal lattice, and a reduction in overall solubility. Along with its anti-demineralization properties, fluoride interacts with enamel to prevent disintegration via remineralization. This technique utilizes partly dissolved enamel crystals as a substrate for mineral deposition from the solution phase, allowing for partial repair of fractured crystals. Fluoride inhibits the bacterial enzyme enolase, thus preventing the production of bacterial acids. Additionally, it indirectly impacts the phosphotransferase system (PTS), which regulates the amount of phosphoenolpyruvate (PEP) produced. As a result, it decreases the quantity of sugar that enters the cell. This occurs due to fluoride entering the cell as hydrofluoric acid (HF), which then dissociates, lowering the intercellular pH and causing cell disruption. Fluoride may impede the cell's ability to remove excess H+, and acidification of the cytoplasm may decrease acid production.[18]

PATIENT SELECTION CRITERIA

Nano Silver Fluoride may benefit the following: 1. Children at high risk of caries have active cavitated caries lesions in either the anterior or posterior teeth without clinical signs or symptoms of pulpal involvement.
2. Children with non-pulp cavitated caries lesions. If possible, radiographs should be used to ascertain the depth of caries lesions.

3. Children with behavioural or special healthcare requirements and cavitated caries lesions, since the application methods are non-invasive and may be administered simply with a micro brush tip.
4. Children from low-income families who cannot afford the costly dental care process.

METHOD OF APPLICATION

According to Valdeci Elias dos Santos Jr et al. (2014), the following Nano Silver fluoride application technique is recommended.[12]

1. There is no need to excavate carious dentin or remove any supporting enamel before applying Nano Silver fluoride. Because excavation may result in a reduction in the proportion of carious lesions.
2. The carious lesion is first cleansed with a wet cotton pellet to eliminate any unpleasant food particles.
3. Isolation of the tooth to be treated with NSF using a cotton roll or gauge piece.
4. Using a sterile micro brush tip, apply two drops of the NSF solution (equal to 10mg) to the carious lesion for about ten seconds.
5. To prevent cross-contamination, a single micro brush was utilized.
6. To get the best effect, the solution was kept on the tooth surface for about 2 minutes.

EVIDENCE-BASED STUDIES OF NANOSILVER FLUORIDE

1. Effectiveness of deciduous dentition

Tirupathi, Sunnypriyathan, et al., 2019 They discovered that when it came to reducing dentine caries formation in primary teeth, the Nano-Silver integrated Sodium Fluoride (NSSF) group had a higher arrest rate (77%) when compared to silver diamine fluoride.[19] This bactericidal ability is essential in primary teeth, which have more permeable as well as lesser enamel covering than permanent teeth, rendering them more endangered to the acidogenic activity of the bacterial leading to formation of carious lesion.[20]

In 2014, Dos Santos VE et al. found that Nano Silver Fluoride is effective when administered yearly. By the seventh day, it hardens and prevents dentine cavities in primary teeth 81 percent more efficiently than a placebo (water). Additionally, he discovered that 66.7 percent of arrest caries occurred by the 12th month. The synergy of the ingredients in Nano Silver Fluoride's composition (chitosan, silver nanoparticles, and fluoride) accounts for the product's anti-caries efficacy.[12]

Zuhair Al-Nerabieah et al. 2020 discovered that a new nano-silver fluoride formulation, including green tea extract, was efficacious in altering the carious lesions in deciduous teeth, with a six-month complete arrest rate (67.4%). Across all follow-up periods, the carious lesions treated with SDF was substantially more arrested than the lesions treated with NSF-GTE. It may be due to the fact that SDF 38% contains noticeably more Silver Nitrate and Sodium Fluoride than NSF-GTE (5x AgNO3 percent, 4x NaF %).[14]

Zuhair Al-Nerabieah et al. 2020 assessed the cariostatic efficacy or the acceptability of Nano Silver Fluoride and SDF in primary teeth of preschool children. After three weeks, 77 percent of arrested carious lesions was found in the NSF group and by six months, the rate had decreased to 67.2%, which was lower than the SDF group. They found that both SDF and NSF successfully reversed carious dentine lesions in preschool children and were well tolerated.[21]

Arnaud M et al. published a study in 2021 comparing the efficacy of two different silver nanoparticle (AgNP) concentrations of nano-silver fluoride (NSF), 400 and 600 ppm, in preventing dental cavities. They concluded that Nano Silver Fluoride containing 600ppm was more efficient than 400ppm.[13]

2. Efficacy of caries arrest at various concentrations

Arnaud M et al. established the effectiveness of two different silver nanoparticle (AgNP) concentrations, 400 and 600 ppm, in 2021. Compared to the NSF 400, the NSF 600 had a success rate of 72.7% in preventing caries, while the NSF 400 had a success rate of 56.5%. The increased concentration of AgNPs in NSF 600 accounts for the higher success rate.[22]

3. Antimicrobial properties

M. Di Guilio et al. (2013) showed the antibacterial activity of Chitlac-nAg, a non-composite system composed of chitosan and silver nanoparticles that serve as a lactose substitute. At 0.1 percent Chitlac-nAg showed an antibacterial effect on almost all the species of streptococcus except S. mitis. At a concentration of 0.2 percent, Chitlac-nAg suppressed bacterial growth in both the supernatant phase and the mature biofilm. Chitlac-nAg has the ability to prevent the development of biofilms in S. mitis even at 0.1% concentration, At much lower concentrations, the adhesion capacity of Streptococcal strains was decreased in a concentration-dependent manner, as was the metabolic biofilm activity.[23]

PLL Freire et al. (2014) showed that smaller AgNPs had the most antibacterial activity against bacteria due to their more extensive contact area with the bacterial cell surface. The ability of AgNPs with different sizes and morphologies to prevent S. mutans biofilms was shown (sphere, triangular and elliptical).[24] Nanoparticles may be utilized to prevent the development of oral biofilms due to their bactericidal and anti-adherent characteristics due to its nanoscale size. Consequently, metallic nanoparticles' strong antibacterial effectiveness has been ascribed to their small size and high surface-to-volume ratio.[3]

4. Action of remineralization

Ali Nozari et al. in 2017 discovered that the NSF group had the highest SMH (surface microhardness) readings

and percent SMHR (percentage of surface hardness recovery), concluding that NSF had the best remineralization efficiency.[25]

In 2018, Amitis Vieira Costa e Silva et al. showed that both Nano Silver Fluoride and Sodium Fluoride are efficient in remineralizing enamel. NSF was more efficient than sodium fluoride in buffering the decrease in pH and adhesion of S. mutans to the enamel surface. NSF is more efficient than Sodium fluorides in treating initial carious lesions due to its remineralization and antibacterial characteristics.[26]

V. Silva et al., 2019 investigated the property of nano silver fluoride in the enamel remineralization process using optical coherence tomography. The nanoparticles of silver do not affect the action of fluoride. This is due to its inherent ionic stability. This finding is significant for deciduous teeth since their enamel has a distinctive feature. The degradation trajectories for the NaF and nano silver fluoride groups were comparable. They concluded that NSF is as effective as sodium fluoride in remineralizing tooth enamel.[27]

In 2020, Abuhashema et al. examined the impact of glass ionomer cement restorations after application of Nano silver fluoride (NSF) solution on residual infected dentin remineralization and also on the tertiary dentin formation after partial caries elimination in occlusal carious molars in 16–35-year-old patients. After six months, both groups saw an increase in dentin density and residual dentin thickness. After six months, the group treated with NSF before GIC repair had a much more significant percentage change in density. However, no variation in the thickness of the tertiary dentin generated was seen between the two groups. NSF enhanced dentin remineralization in carious dentin, indicating its role in caries arrest.[28]

In 2021, El-Desouky et al. evaluated the anti-cariogenic efficacy of Nano Silver Fluoride (NSF) in combination with fluoride varnish (FV) on primary tooth enamel. They found that applying NSF and FV to teeth before the acidic challenge positively impacted demineralization. NSF and FV-treated groups exhibited the most excellent microhardness ratings and the smallest lesion depth values. As a consequence of these findings, it was shown that NSF was equally effective as an anti-cariogenic agent capable of preventing enamel demineralization.[29]

5. Effect on the development of plaque biofilms

Sri Angky Soekanto et al. investigated the effectiveness of NSF and propolis fluoride (PPF) for reducing biofilm development in Streptococcus mutans and Enterococcus faecalis. And found that NSF and PPF decreased the formation of biofilms in proportionate to dosage used. As a result, it was determined that fluoride-based varnishes such as NSF and PPF had a significant antibacterial effect.[30]

6. Efficacy of Secondary Caries Prevention

Nanda K J et al. 2020 discovered that pre-treated cavity which were filled with GIC and composite had significantly greater mean microhardness values than the cavity that were filled without pre-treatment using NSF. This result was suggestive of the remineralizing effect of NSF. The pre-treated group showed a decreased in outer lesion depth, suggesting better tooth restoration stability. Consequently, it was found that pre-treatment of GIC and composite resin restorations with NSF increases their resistance to secondary caries formation.[31]

7. Staining characteristic

Espindola-Castro, LF et al. found in 2019 that Nano Silver fluoride at concentrations of 600ppm and 1500ppm caused a light-yellow stain on the enamel surface, which in turn decrease the brightness. This staining may result from the addition of chitosan to the mixture, which may have aided in the formation of this film, which is easily removed.[32]

8. Cytotoxicity

Targino et al. (2014) showed in 2014 that Nano Silver Fluoride had no impact on the erythrocyte membrane of human erythrocytes independent of blood type. When absolute cytotoxicity levels were examined, it was shown that Nano Silver Fluoride was less harmful than Silver Diamine Fluoride. It also has the lowest inhibitory and minimum bactericidal concentration with a potent antibacterial action.[33]

ADVANTAGES

1. Nano Silver fluoride can arrest carious lesions in primary teeth.
2. It is a form of non-invasive treatment to arrest dental caries as no carious lesion excavations are required.
3. It does not stain the tooth because of the incorporation of nano Silver which does not form silver oxide when exposed to air or oxygen.
4. It also can remineralize and prevent the progression of secondary caries.
5. It also has an antimicrobial property which further prevents dental biofilm formation of the tooth surface.
6. It requires minimum armamentarium to apply on the tooth surface
7. It is cost-effective

SIDE EFFECT / ADVERSE EFFECT

According to Targino et al. in 2014, Nano Silver fluoride poses no systemic toxicity and poses no health hazard. Thus, concluding that Nano Silver fluoride is safe to use for the treatment of the carious lesion.[33]

CONCLUSION

NSF can be an ultimate and excellent way of arresting the carious lesion when administered directly to caries lesions with the aesthetic outcome by eliminating the drawbacks of discoloration with Silver Diamine Fluoride (SDF). The NSF application is non-invasive, harmless,

and inexpensive, and it may be used safely in both children and adults without obstructing dental health treatment. However, further research is needed to determine the characteristics' long-term efficacy using a large sample size.

CONFLICTS OF INTEREST

The authors disclose that they do not have any conflicting interests.

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