

Nano Silver Fluoride - Overview

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ABSTRACT

Dental caries is a worldwide public health problem disturbing numerous communities. Topical fluorides have been commonly used for caries prevention and arrest. Being one of the most prevalent diseases affecting mankind in both developing and developed nation, the need for materials to establish a healthy balance between pathological and protective factor has urged for the origin of newer silver compound, Nano silver fluoride (NSF), as an alternate to overcome to drawbacks of topical fluoride and Silver Diamine Fluoride (SDF) in caries prevention. This paper aims to give an overview of the properties, indications, contraindications, advantages and disadvantages of Nano Silver Fluoride (NSF) in comparison to other recently used materials.

KEYWORDS: *Silver diamine fluoride, nano silver fluoride, nano silver diamine fluoride, remineralizing agent, antibacterial agent, topical fluorides*

INTRODUCTION

Dental caries, a preventable chronic disease develops from a persistent cycle of demineralization and remineralization. Many treatment modalities have been used in the past to manage early enamel carious lesions. Topical fluorides known for their excellent cariostatic efficacy were the most commonly employed remineralizing agent in mid twentieth century^[1]. In spite of their efficacy and cost effectiveness, topical fluorides necessitate patient cooperation and multiple applications during a year; therefore alternative preparations providing further benefits could be of interest ^[2]

In the 1840s, Silver nitrate was first reported as an effective agent in arresting carious lesions^[3] for which G.V Black described protocols for its use in the early 1900s^[4]. This paved the way for newer product containing silver; Silver diamine fluoride (SDF). It has proven antibacterial action that releases fluoride ions quickly, therefore, assisting enamel remineralization. It is recommended as a valuable caries preventive intervention by dentists in Japan, India, Australia, and United States. Today, Silver diamine fluoride (SDF) is available for arresting caries as a simple, non-invasive, and low-cost medication with more efficacy and superiority than fluoride varnish^[5]. Despite the ability of SDF in preventing and

arresting caries even when applied annually, it has few disadvantages such as blackish staining of teeth and metallic taste^[6, 7, 8].

The need for newer materials with esthetic concern and establishment of a healthy balance between pathological and protective factors has led to the discovery of newer silver compounds, such as Nano Silver Fluoride (NSF)^[9, 10]. NSF has been suggested as an alternative to Silver Diamine Fluoride (SDF) by many authors^[6, 7, 8]. It is described as an eco friendly, low cost material, with the shelf life of 3 years that is effective in arresting dental caries^[11, 12]. This paper aims to evaluate the efficiency of the newer material Nano Silver Fluoride (NSF) as a non-invasive treatment option for various clinical conditions.

Silver Nanoparticle

Nanotechnology is fast emerging in the 21st century due to its economic and scientific potential and is experiencing rapid growth with many potential applications in dentistry^[13]. Due to its unique characteristics, Silver Nanoparticles (AgNPs) with a high specific surface area and a high fraction of surface atoms have attracted the attention^[14]. Silver Nanoparticles (AgNPs) are one of the most widespread consumer products known for their antimicrobial properties^[15]. Several patents claim that formulations containing such entities can be used for caries arrest and oral care^[16, 17].

Particles size (3.2–1.2 nm)

Shape - spherical

Nano Silver Fluoride

Nano Silver Fluoride is a new experimental formulation containing AgNPs, chitosan, and fluoride. It is similar to SDF with combined preventive and antimicrobial properties. In order to combat the drawbacks of discolouration it has been developed as an effective anticaries agent with esthetic concern^[11]

Composition

1. Chitosan (28,585 µg/ml); - stabilizing agent of the colloid^[18]
2. Silver (376.5 µg/ml);
3. Sodium fluoride (5028.3 µg/ml)^[19]

Mechanism Of Action

Nano silver based preparations are gaining popularity as excellent anti-bacterial, anti-fungal and anti-viral agents^[20]. The action of NSF in the arrest of caries can be demonstrated by the synergism of the components, chitosan, AgNPs, and fluoride formulation. Silver is typically used nitrates form to cause antimicrobial effects, but when AgNPs are used, the surface area available for exposure to the microbe is greatly increased^[21]

The possible mechanisms of action of Nano-silver are due to better contact with the microorganisms. Nanometre scale silver provides an extremely large area of contact with bacteria. The nanoparticles get attached to the cell membrane and penetrate the bacteria. Bacterial membrane with sulphur-containing proteins and AgNPs like Ag⁺, can interact with them as well as with phosphorus-containing compounds like DNA, perhaps to inhibit the function. Silver nanoparticles (AgNPs) can attack the respiratory chain in bacterial mitochondria and lead to cell death^[22]. AgNPs tend to possess a sustained release of Ag⁺ once inside the bacterial cells, which can create free radicals and induce oxidative stress, further enhancing

their bactericidal activity as suggested by **Danilcauk and Kim**^[23]. Such interactions in the cell membrane would prevent DNA replications, which would lead to bacterial death^[20]

Several studies indicate that AgNPs antibacterial mechanism relies on their ability to penetrate the bacterial cell wall, resulting in direct and indirect lipid peroxidation which destroys the cell membrane, disrupts the replication of DNA, and restores and inhibits the respiratory protein^[24]

Action On Deciduous Teeth

Silver nanoparticles (AgNPs) accumulate in the bacterial membrane, causing a significant increase in permeability, resulting in the death of the cell^[25]. This bactericidal ability is especially important in deciduous teeth, as they have a thinner and more permeable enamel layer than permanent teeth and they are more vulnerable to the acid action of these bacteria and, therefore, more susceptible to dental caries^[26]. The NSF-prevented fraction of caries arrest in the primary teeth was similar to Silver Diamine Fluoride (SDF) prevented fraction reported in the clinical trial conducted by **Llodra et al** (2005)^[27].

Valdeci Elias (2017) found that the annual application of Nano Silver Fluoride was more effective in hardening and arresting dentine caries in primary teeth than the placebo^[11].

Prevention Of Biofilm Formation

Nano-silver has the ability to inhibit biofilm formation by suppressing growth of biofilm forming bacteria^[28, 29, 30]. Antimicrobial efficacy of Nano-silver is inversely proportional to the dimensions of Silver nano particles i.e., lesser the dimension, higher the antimicrobial efficacy^[31]. Particles smaller than 10 nm are considered to possess a high performance against pathogens of the dental biofilm. Formation of oral biofilm could be controlled by nanoparticles because of their biocidal and anti-adhesive microbial capabilities. Fundamentally, particles are reduced from micrometer to nanometer size, altering active surface area, hardness, chemical reactivity and biological activity. For this reason, with respect to metallic nanoparticles, the biocidal effectiveness has been suggested to be due to both their size and high surface-to-volume ratio^[25].

Freire et al (2015), in a study reported that AgNP colloids inhibited *S. Mutans* biofilm formation on bovine enamel surfaces^[28]

ANTICARIOGENICITY

Valdeci Elias (2017), investigated the effectiveness of Nano Silver Fluoride (NSF) as anti-caries agent with water a control, applied once a year to arrest caries in decayed primary teeth and reported it to be effective in arresting active dentine caries, without any distinctive tissue darkening due to the oxidation of silver ions when in contact with the teeth. The effectiveness of Nano Silver Fluoride (NSF) in the caries arrest is attributed to the synergistic action of silver nanoparticles and fluoride. However, the mechanism of arrestment is not clear^[11].

Various studies showed that chitosan and silver nanoparticles have antimicrobial activity against mutans streptococcus and lactobacillus, pathogens mainly responsible for the initiation and development of carious lesions, respectively^[24, 33]. Further, the tiny size of the NSF nanoparticles and their spherical shapes potentiate the antimicrobial effect by increasing the contact surface^[34, 35]

Haghgoo and co-workers^[29] suggested the incorporation of Nano-silver in varnishes and reported increased antimicrobial properties against cariogenic microorganisms such as *S. mutans*^[18] and *S. salivarius*.

Studies have reported the antimicrobial action of silver nanoparticles on Gram-positive and Gram-negative bacteria, showing bactericidal effects on microorganisms, such as *Escherichia coli* [36, 37, 31], *Staphylococcus Aureus* [37], *Enterococcus faecalis* [31] and *S. Mutans* [39, 31].

Furthermore, silver nanoparticles–fluoride colloids are potential options for the control of multidrug-resistant microorganisms and do not represent substantial risks to human health [33, 40].

Santos et al (2014) [11] investigated the efficacy of Nano Silver Fluoride (NSF) in comparison with water in a randomized control trial. He emphasized that Nano Silver Fluoride (NSF) was an effective agent in preventing and arresting dental caries in underdeveloped countries but the effect on caries should be investigated with alternative evaluation methods as well.

Asmaa Aly Abo El Soud (2020), evaluated and compared the effects of Silver Diamine Fluoride (commercial and lab prepared) versus Nano silver fluoride (NSF) on demineralized human enamel surfaces of premolars extracted for orthodontic reasons and concluded that NSF is more efficient than Silver Diamine Fluoride (SDF) (lab made & commercial form) on demineralized enamel surfaces. [19]

REMINERALIZING AGENT

Although the antibacterial activities of silver nanoparticles are well known, **Scarpelli et al (2017)** in a study on remineralization effect of AgNPs, concluded that Ag-Nano particles re-mineralized deciduous dental enamel and showed bactericidal activity against *S. mutans*, *E. faecalis* and *E. coli* [42]

Esilva et al in 2018 reported that Nano Silver Fluoride (NSF) was found to be simpler and more effective than conventional fluorides in treating incipient caries lesions due to its remineralizing potential. Nano Silver Fluoride (NSF) had greater effectiveness compared to sodium fluoride (NaF) in preventing lowering of pH and adhesion of *S. mutans* to the enamel surface. Higher interference on *Streptococcus mutans* adhesion to the enamel surface and higher inhibition on *S. Mutans* acidogenicity than NaF has been reported [18]

Akyildiz M et al, 2019 assessed the remineralization effect of an experimental Nano Silver Fluoride (NSF) formulation using an in vitro remineralization model and compared it with Silver Diamine Fluoride (SDF) and sodium fluoride varnish (NaF) in sound human third molars and concluded that NSF wasn't found to be effective as sodium fluoride varnish and SDF on artificial enamel caries lesion. He stated that further investigations are needed to recommend the use of NSF as an alternative agent to routine fluoride treatment [41]

Currently there is not enough data about the penetration depth rates of AgNPs through enamel and also their effects of their sizes and shapes on enamel remineralisation in literature.

Biocompatibility

The Nano Silver Fluoride (NSF) was not toxic at any concentration tested for any type of erythrocyte and is more biocompatible than Silver diamine fluoride (SDF). **Targino et al. (2014)** during a study evaluated cytotoxic activity of Nano Silver Fluoride (NSF) in comparison with chlorhexidine and silver diamine fluoride and reported that the NSF is a bacteriostatic and bactericidal compound with statistically significant difference in minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) values [12].

Microhardness

Nano Silver Fluoride (NSF) caused a statistically significant increase in surface hardness values compared to control group but significantly lower microhardness values in comparison with Silver Diamine Fluoride (SDF) and Sodium fluoride (NaF) groups in a study by **Akyildiz M et al, 2019** [41]. The higher surface microhardness values of Silver Diamine Fluoride (SDF) compared to Nano Silver Fluoride (NSF) might be related to SDF's pH (**Mei et al**)^[43]

Ease Of Application

The treatment procedure is simple, less technique sensitive^[44]and does not requires any dental equipment or a clinical setting ^[11]

Advantages

Non-invasive procedure and the risk of cross-infection is significantly reduced. No adverse effects has been reported as of now ^[11]

Nano Silver Fluoride (NSF) does not cause immediate dark staining of dentinal tissue. The reason being alteration of their chemical reactivity due to their particle size, nano silver does not form oxides ^[44, 42]

Metallic taste, painful ulceration have not been reported yet^[44]

The chemical reactivity of silver nano particles was altered such that the colloid is unable to stain the teeth black. Chitosan being an adjuvant, prevents enamel mineral loss during pH cycling as it can positively affect in vitro enamel demineralization, preventing the loss of ions, especially from hydroxyapatite ^[42]. Moreover, **Freire et al** reported that Silver nanoparticles (AgNPs) do not promote colour change in dental enamel, which is an aesthetic advantage compared with traditional silver products ^[28]

Cytotoxicity

Cytotoxic studies reported that Nano-silver has lower cytotoxicity when compared to other dental materials ^[12, 45].

Freire et al (2015), in his study evaluated the cytotoxicity of silver nanoparticle (AgNPs) colloids on dental enamel and reported that they have a lower concentration of silver, with low toxicity and bactericidal effect against a cariogenic oral bacterium^[28]

Cost Effectiveness

NSF application is inexpensive and thus can be reliable and afforded by most communities ^[11]

5% NSF is eight times economical compared to 38% SDF (**Tirupathi et al in 2019**). Hence, its use at community level is cost effective and reliable ^[43].

CONCLUSION

Nano Silver Fluoride (NSF) is considered to be an effective alternative for caries arrest and treatment with an esthetic advantage overcoming the drawbacks of discolouration on use of Silver Diamine Fluoride (SDF) when applied directly to caries lesions. NSF application is noninvasive, nontoxic and cost effective and can be safely used in children and adults without imposing barriers to oral health care. However additional studies are required to determine long-term effectiveness of its properties with large sample size.

Ethical clearance – Not applicable

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Conflict of interest – nil

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