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Advances in Fluoride Clinical Applications in Dentistry

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Abstract: Fluoride plays an important role in caries prevention, but conventional agents each has its own drawbacks. Advances in nanomaterials and related technologies have changed that picture: nanosilver fluoride (NSF) keeps the antibacterial and remineralization benefits—and it avoids the staining issue. NSF performs well in caries management, orthodontic white spot lesion prevention, and dentin desensitization. It may therefore serve as a promising alternative to silver diamine fluoride. Fluoride-containing bioactive glass (FBG) can slowly release calcium, phosphorus, and fluoride ions. This supports durable remineralization and excellent dentinal tubule occlusion. FBG is promising for caries prevention and desensitization therapy; its mechanical properties, however, still need improvement. In addition, novel materials such as copper tetraamine fluoride, silver complex fluoride, nano calcium fluoride composites, and strontium-containing fluorapatite have also demonstrated considerable antibacterial and remineralization potential. The long-term safety and optimal application protocols of these novel materials still warrant further clinical investigation.

Keywords: Fluoride; Caries Prevention; Nanosilver Fluoride; Fluoride-containing Bioactive Glass; Remineralization.

1. Introduction

Fluoride plays a vital role in maintaining dental health and preventing dental caries, serving as the first line of defense against the development of tooth decay [1]. The applications of fluoride encompass caries prevention, management of orthodontic demineralization, adjunctive periodontal therapy, and intervention for dentin hypersensitivity, among other domains. Nanotechnology, materials science, and biomimetics are now used together. This has gradually improved how fluoride is released, how well it remineralizes, and how safe it is. These gains help offset the limitations of conventional formulations; they also offer new directions and material options for clinical oral diagnosis and treatment.

2. Clinical Applications of Commonly Used Inorganic Fluorides in Dentistry

Topical fluoride acts through several pathways—not just one. It slows dental demineralization and helps demineralized tissue remineralize; it also disrupts carbohydrate metabolism in cariogenic oral bacteria and weakens plaque biofilm activity [2]. Commonly used inorganic fluorides include sodium fluoride, sodium monofluorophosphate, stannous fluoride, and silver diamine fluoride. Not all fluorides behave alike; their physicochemical properties and biological effects can differ markedly. With long-term use, the advantages and limitations of each have gradually come into sharper focus.

2.1. Clinical Applications of Sodium Fluoride in Dentistry

Sodium fluoride (NaF) is one of the earliest fluoride agents used in the treatment of dental caries, and its effects exhibit a typical concentration-dependent pattern.Low concentrations of NaF are commonly delivered through toothpastes, mouthrinses, and professionally applied varnishes. At these levels, NaF effectively reduces caries incidence; it also arrests the progression of early carious lesions—an effect driven largely by promoting remineralization [1].High concentrations of NaF, however, produce marked adverse effects. Long-term intake of high-concentration NaF not only causes dental fluorosis but also exerts cytotoxicity on various oral cells, inducing oxidative stress and apoptosis, while higher doses may lead to skeletal fluorosis [3]. In the pathological environment of periodontitis, high-concentration NaF promotes macrophage polarization toward the pro-inflammatory M1 phenotype, thereby exacerbating inflammation and alveolar bone resorption and potentially interfering with periodontal tissue healing [4].

2.2. Clinical Applications of Sodium Monofluorophosphate in Dentistry

Sodium monofluorophosphate (SMFP) is a widely used fluoride-containing component in toothpastes.It is compatible with common toothpaste abrasives like calcium carbonate and silica; it doesn't readily precipitate or lose activity. It is also cheap, and it won't stain teeth.However, SMFP requires decomposition by oral bacteria and enzymes to release free fluoride ions before it can exert its effect, and its overall rate of action is relatively slow [5].

2.3. Clinical Applications of Stannous Fluoride in Dentistry

Stannous fluoride (SnF_2) can inhibit oral biofilm activity, promote the remineralization of dental hydroxyapatite, and occlude dentinal tubules, thereby effectively alleviating the symptoms of dentin hypersensitivity [6]. However, stannous ions are susceptible to oxidation and discoloration, causing transient grayish-yellow or brown staining on tooth surfaces and imparting a distinct metallic taste; moreover, the product exhibits poor storage stability and its activity readily declines [7].

2.4. Clinical Applications of Silver Diamine Fluoride in Dentistry

Silver diamine fluoride (SDF), which contains fluoride and silver ions, is a cost-effective anticaries agent [8] and has gained broad recognition in the global dental field. 38% SDF inhibits MMP-2, MMP-8, and MMP-9, which blocks dentin caries progression [9]. SDF also shows positive caries-preventive effects—on intact anterior tooth surfaces and on cavities in permanent teeth [10]. Yet SDF has a notable drawback: it leaves permanent stains on teeth, ranging from brown to black, which has kept it from being widely adopted. This is where glutathione (GSH) comes in. GSH is a key intracellular antioxidant; it helps reduce oxidative stress and may also have a whitening effect. Indeed, Sayed et al. found that adding 20% GSH to SDF reduced staining on the tooth surface [11][12].

3. Clinical Applications of Nanosilver Fluoride in Dentistry

Nanoscience and nanotechnology have helped give rise to nanosilver fluoride (NSF), a new material for fighting caries. Tarantino et al. used a chemical reduction method to reduce silver nitrate. Chitosan served as the carrier and fluoride as the stabilizer; together, these components enabled them to prepare NSF successfully for the first time [13]. Haghgoo et al. prepared an anticaries varnish by mixing silver nanoparticles (AgNPs) with NaF varnish [14]. In NSF, chitosan blocks the adhesion of Streptococcus mutans. This inhibits dental biofilm formation [15] and reduces demineralization. Fluoride ions also slow mineral loss and promote remineralization. They form an acid-resistant fluorapatite layer, which helps prevent caries [16].

3.1. Applications of Nanosilver Fluoride in Caries Prevention and Treatment

NSF is biocompatible. It doesn't stain teeth or corrode tissue, and it fights caries better than conventional fluorides and SDF [17].In vitro studies show that NSF boosts enamel surface microhardness and promotes remineralization [18]. It also raises the bioavailability of silver, fluoride, calcium, and phosphorus in saliva, which strengthens its antibacterial and remineralizing effects [19].Multiple studies have shown that NSF can effectively inhibit caries progression without blackening teeth and has higher parental acceptance; its caries-preventive effect in children with special health care needs is comparable to that of SDF, and after pretreatment, it can effectively inhibit the development of secondary caries in restored teeth, thus making it an ideal alternative to SDF [20]-[22].

Tarantino et al. evaluated the cytotoxicity of NSF based on its hemolytic activity against human erythrocytes and found that it was non-toxic at concentrations of 100, 50, 25, 12.5, and 6.25 μg/mL [13]. However, the cytotoxicity of NSF to dental pulp cells and its long-term biosafety remain unclear, and systematic in vivo studies and large-sample clinical evidence are lacking.

3.2. Applications of Nanosilver Fluoride in Orthodontic Caries Prevention and White Spot Lesion Prevention

Orthodontic patients with appliances often have areas that are hard to clean, so plaque builds up and enamel begins to demineralize early. Pretreating the enamel with specific anticaries agents before treatment can effectively prevent white spot lesions.Aya et al. combined NSF with a diode laser for enamel pretreatment, which significantly enhanced the acid resistance and anticaries effect of enamel around brackets [23]. A nanosilver fluoride sustained-release orthodontic elastomer (NSF-RE) releases both antibacterial silver nanoparticles (AgNPs) and fluoride that promotes remineralization [24]. It also inhibits various bacterial biofilms and enamel demineralization, which helps reduce the incidence of white spot lesions [25].In addition, a colloidal chitosan-silver nanoparticle-fluoride nanocomposite (CCAgNPF) mouthrinse exhibits an antibacterial effect similar to that of 0.2% chlorhexidine mouthrinse, and the combination of the two shows the most favorable antibacterial performance [26]. However, most current evidence comes from in vitro experiments and preliminary clinical studies; long-term follow-up data from large cohorts are still lacking.

3.3. Applications of Nanosilver Fluoride in Periodontal Tissue Regeneration

In the treatment of periodontitis, guided tissue regeneration (GTR) membranes selectively separate different periodontal tissues, prevent the gingival epithelium and gingival connective tissue from growing toward the root surface, and induce the growth and differentiation of periodontal ligament cells with regenerative potential, thereby achieving regeneration of the periodontal ligament, alveolar bone, and cementum [27]. Microbial contamination in the GTR surgical area can compromise treatment outcomes and is detrimental to the regeneration of connective tissue and bone. AgNP-loaded GTR dressings reduce bacterial adhesion and invasion, thereby facilitating the treatment of intrabony defects and improving clinical prognosis [28]. An in vitro study developed an NSF-coated silk fibroin GTR membrane. It showed strong antibacterial activity, favorable biomineralization, good biocompatibility, and suitable mechanical properties, suggesting promise for guided tissue regeneration [29].But studies on NSF in periodontal tissue regeneration remain limited, and its safety and long-term efficacy require further validation.

3.4. Applications of Nanosilver Fluoride in Dental Restoration and Pit-and-Fissure Sealing

Shear bond strength is an important factor in ensuring long-term stable integration between restorations and tooth structure and in ensuring durable restorative outcomes, and is crucial to restorative success. In one in vitro study, carious dentin surfaces were treated with nanosilver fluoride–Moringa oleifera leaf extract (NSF-MOLE); the resin composite showed the highest shear bond strength, suggesting that this treatment may improve bonding to composite resin restorations [30]. With resin-modified glass ionomer restorations, NSF-treated specimens looked better aesthetically than SDF-treated ones, and neither treatment compromised the shear bond strength of the restorations [31]. In addition, both NSF and SDF can serve as effective pretreating agents to enhance the performance of pit-and-fissure sealants in primary teeth, with NSF achieving higher shear bond strength and superior marginal sealing [32].

3.5. Applications of Nanosilver Fluoride in Tooth Desensitization

Molar incisor hypomineralization (MIH) may lead to tooth hypersensitivity. A clinical study confirmed that NSF can alleviate MIH-related tooth sensitivity and rapidly relieve pain; moreover, NSF has a more sustained effect in alleviating tooth sensitivity and can effectively inhibit plaque formation, showing superior overall performance [33].

4. Clinical Applications of Fluoride-Containing Bioactive Glass in Dentistry

Traditional bioactive glass (BG), owing to its unique advantage of forming stable chemical bonds with bone tissue and dental hard tissues, has become a subject of extensive interest and intensive investigation [34]. Adding fluoride to the glass network creates new functional possibilities and broadens the material's potential uses, while its intrinsic bioactivity stays intact. Fluoride-containing bioactive glass (FBG) is a type of degradable silicate-based glass [35]. When dissolved in aqueous solution, it releases silicon, calcium, phosphorus, and fluoride ions, thereby exerting remineralization effects. Fluoride ions exist in charged forms such as CaF^{+} within the glass system, which enables FBG to preserve the connectivity of the glass network and achieve controlled sustained release of fluoride ions [36].

4.1. Applications of Fluoride-Containing Bioactive Glass in Caries Prevention and Treatment

Enamel demineralization marks the onset of caries. An in vitro study using a pH-cycling model found that toothpaste containing FBG significantly slowed enamel demineralization, and the effect was closely related to the material concentration [37]. Formulating FBG as a varnish (especially a modified version incorporating nanosilver) and applying it to the surface of carious lesions effectively promoted mineral deposition and hardness recovery in demineralized enamel, with remineralization effects comparable to or even better than those of conventional fluoride varnish [38]. These findings point to a possible role for FBG as a remineralizing restorative material in minimally invasive dentistry. In a separate in vitro study, toothpastes with different fluoride levels were tested against root caries. The bioactive glass toothpaste with 540 ppm fluoride released more calcium and phosphate, and it rehardened root caries lesions more effectively [39]. Fluoride-containing bioactive glass toothpaste is effective in arresting root caries; however, more clinical practice is needed to validate this finding.

4.2. Applications of Fluoride-Containing Bioactive Glass in the Prevention and Treatment of Dentin Hypersensitivity

Hydrodynamic theory holds that relieving dentin hypersensitivity mainly depends on blocking exposed dentinal tubules. FBG achieves this physically: apatite crystals form on its surface and deposit at the tubule openings and inside the lumens, thereby occluding the tubules. Lynch et al. confirmed that after FBG treatment, the surfaces of dentin specimens were completely covered with apatite crystals, the openings of dentinal tubules were completely occluded, and this effect remained stable for 7 days [40]. Compared with fluoride-free bioactive glass, FBG occludes tubules more rapidly, forms a denser and firmer apatite layer, and exhibits greater sealing stability. Moreover, FBG has good biocompatibility and is non-cytotoxic to human periodontal ligament stem cells and oral fibroblasts, supporting its long-term safe clinical application [41]. The fluoride-containing bioactive glass toothpaste BioMin® F (fluoro calcium phosphosilicate, FCPS) demonstrated superior desensitizing efficacy to NaF varnish at 3 and 6 months [42] and effectively reduced dentin permeability, indicating good application potential in ameliorating acid erosion-related dentin hypersensitivity [43]; furthermore, FBG effectively alleviated enamel sensitivity under gastric acid erosion [44]. However, the long-term sealing stability of FBG in the complex oral environment still requires validation.

4.3. Applications of Fluoride-Containing Bioactive Glass in Orthodontic Caries Prevention and White Spot Lesion Prevention

During orthodontic treatment, improper cleaning around brackets can readily cause enamel demineralization and the formation of white spot lesions. In vitro studies have shown that FBG composites can achieve long-term sustained release of F^{-}, Ca^{2+}, and PO_4^{3-}, showing potential for preventing demineralization of dental hard tissues around orthodontic brackets [45]. Adding FBG to composite resin adhesives led to fluorapatite formation at low pH, and the amount increased over time [46]. This suggests that these adhesives may help prevent and repair enamel white spot lesions. In addition, BioMin F toothpaste combined with a diode laser significantly promoted the remineralization of demineralized enamel [47], and its combined application with orthodontic brackets effectively reduced the incidence of enamel white spot lesions around brackets.

4.4. Applications of Fluoride-Containing Bioactive Glass in Enhancing Restoration Durability

Improving the durability of bonded restorations and prolonging their intraoral service life are important research directions in contemporary dentistry. In vitro studies suggest that Biomin F paste, when used as a temporary filling, can improve the durability of dental restorations and help preserve demineralized tooth structure during cavity preparation for caries—thereby protecting the tooth [48]. Simulated toothbrushing experiments have shown that FBG-containing toothpaste has minimal effect on the appearance of restorations [49].

5. Clinical Applications of Other Novel Fluorides in Dentistry

Current research has centered on new fluoride formulations, better delivery systems, and synergistic ingredients. The goal is to make dental hard tissues more resistant to caries while keeping side effects to a minimum. These approaches—nanofluoride carriers and highly bioavailable fluoride composites, among others—have shown promise for clinical translation, especially for enamel remineralization and for modulating oral microbial activity.

5.1. Novel Copper Tetraamine Fluoride

An in vitro study developed a novel copper tetraamine fluoride (CTF) using copper fluoride and ammonia solution. The study showed that this material has good biocompatibility and does not cause tooth discoloration, while effectively inhibiting the colonization and growth of Streptococcus mutans biofilms on human dentin surfaces [50]. A separate study found that CTF improved remineralization and repair in artificially carious dentin [51].

5.2. Novel Silver Fluoride Complexes

A novel silver complex fluoride (SCF) was prepared by combining silver fluoride with 1,3,5-triaza-7-phosphaadamantane (PTA). In vitro, it inhibited Streptococcus mutans biofilm growth and showed strong antibacterial activity. Compared with SDF, it was less toxic to human gingival fibroblasts and stem cells from deciduous teeth, and it barely stained teeth [52]. Another study confirmed that the novel SCF significantly reduced the demineralization depth of carious lesions and decreased dental mineral loss [53].

5.3. Novel Calcium Fluoride Complexes

A novel pit-and-fissure sealant material containing composite nano calcium fluoride ($nCaF_2$) and antibacterial monomers can release fluoride ions in a sustained and stable manner, possesses excellent remineralization potential, and simultaneously exhibits ideal mechanical strength, marginal sealing, and good biocompatibility [54]. Another in vitro study developed CaF_2-coated orthodontic O-rings. These rings improved fluoride release and reduced the burst effect; they also kept the O-rings' elasticity and mechanical strength intact—offering a valuable new strategy for preventing orthodontic white spot lesions in clinical practice [55].

5.4. Strontium-Containing Fluorapatite

Hong et al. developed orthodontic adhesives incorporating strontium-containing fluorapatite (Sr-FAp), fluorapatite (FAp), and strontium-containing hydroxyapatite (Sr-HAp). This material steadily releases four ions—calcium, phosphorus, strontium, and fluoride—for up to 60 days; this forms a fluorapatite-like mineralized layer on the tooth surface. It also supports strong remineralization without weakening bond strength, helping prevent orthodontic white spot lesions from forming and progressing [56].

6. Summary and Outlook

Fluoride is an important tool for preventing and controlling caries. Traditional fluorides rely only on fluoride ions to remineralize; as a result, they are limited in controlling active carious lesions. NSF—modified through nanotechnology—gets around the staining problem of silver fluoride agents and offers strong antibacterial and anticaries effects. Still, its optimal concentration, how often it should be used, and its long-term safety remain to be established. FBG releases calcium, phosphorus, and fluoride ions steadily. This supports sustained remineralization with low fluoride exposure; however, its mechanical properties are relatively poor, and its long-term stability still needs verification. More recently, various novel fluorides have been used more widely in pediatric caries management, protecting special populations, and preventing orthodontic demineralization. As materials and clinical research move forward, fluoride use will shift gradually from caries prevention alone to comprehensive oral care—combining prevention, treatment, and restoration.

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