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Fluoride and Nanotechnology in Preventive Dentistry: A Narrative Review of Recent Advances

Fluoruro y nanotecnología en odontología preventiva: una revisión narrativa de los avances recientes

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Abstract:

Dental caries remains the most prevalent chronic disease worldwide, necessitating continuous advancements in preventive dentistry. Fluoride-based agents and nanotechnology-enhanced materials–most notably nano-hydroxyapatite (nano-HA)–have demonstrated significant potential for enamel and dentin remineralization. While fluoride inhibits demineralization and promotes mineral recovery through integration into the apatite structure, nano-HA leverages its nanoscale dimensions to penetrate dentinal tubules and facilitate structural restoration. The incorporation of nanoparticles into glass ionomer cements (GICs), resin sealants, and silver diamine fluoride (SDF) has been associated with enhanced mechanical properties, sustained fluoride release, and potent antibacterial activity. Clinical evidence supports their efficacy in caries prevention, the management of dentin hypersensitivity, and biofilm mitigation. However, concerns persist regarding the potential cytotoxicity of specific nanoparticles and the current scarcity of long-term clinical data. This narrative review synthesizes contemporary evidence on fluoride and nano-HA in preventive dentistry, emphasizing their mechanisms of action, clinical performance, biocompatibility, and future perspectives.

Keywords:

Dental caries, Fluoride, Nano-hydroxyapatite, Nanoparticles, Preventive dentistry, Remineralization

Resumen:

La caries dental continúa siendo la enfermedad crónica más prevalente a nivel mundial, lo que impulsa avances constantes en la odontología preventiva. Los agentes fluorados y los materiales potenciados con nanotecnología, especialmente la nanohidroxiapatita (nano-HA), han demostrado un alto potencial para la remineralización del esmalte y la dentina. El fluoruro inhibe la desmineralización y favorece la remineralización al integrarse en la estructura de apatita, mientras que la nano-HA, debido a su tamaño nanométrico, penetra eficazmente en los túbulos dentinarios y promueve la restauración mineral. La incorporación de nanopartículas en cementos de ionómero de vidrio, sellantes resinosos y fluoruro diamino de plata se ha asociado con mejoras en las propiedades mecánicas, la liberación de fluoruro y la actividad antibacteriana. La evidencia clínica respalda su eficacia en la prevención de caries, el manejo de la hipersensibilidad dentinaria y la reducción del biofilm. Sin embargo, persisten preocupaciones sobre la citotoxicidad de algunas nanopartículas y la limitada evidencia clínica a largo plazo. Esta revisión narrativa sintetiza la evidencia actual sobre el uso de fluoruro y nano-HA en odontología preventiva, destacando sus mecanismos de acción, eficacia clínica, biocompatibilidad y perspectivas futuras.

Palabras Clave:

Caries dental, Fluoruro, Nanohidroxiapatita, Nanopartículas, Odontología preventiva, Remineralización

INTRODUCTION

Dental caries remains the most prevalent disease worldwide and continues to be a major public health challenge, prompting continuous advancements in dentistry to improve preventive and therapeutic strategies. It is a persistent condition of multifactorial origin and variable progression, resulting from an imbalance between dietary factors and the oral biofilm, which leads to the gradual demineralization of dental hard tissues.[1]

Among professionally applied preventive agents, fluoride gels

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are recognized as one of the most effective strategies for caries prevention, reducing caries incidence by approximately 20% in primary dentition and 28% in permanent dentition. However, despite these proven benefits, their administration requires careful consideration of the safety profile, particularly regarding acute or chronic fluoride toxicity. [1]

Acute fluoride toxicity is typically associated with the accidental ingestion of high concentrations and is estimated to occur at a Probably Toxic Dose (PTD) of approximately 5 mg/kg of body weight. At such levels, fluoride interferes with metabolic enzymes and electrolyte balance, potentially leading to gastrointestinal distress and systemic disturbances.[2] In contrast, chronic fluoride toxicity −which is of greater relevance in the dental field− results from prolonged and repeated exposure to subacute fluoride doses. Clinically, this chronic exposure manifests primarily as dental fluorosis, a hypomineralization defect characterized by altered ameloblast function during enamel formation. The risk of fluorosis is influenced by cumulative fluoride intake from multiple sources, including drinking water, dentifrices, and professional preventive modalities such as gels, varnishes, and other topical agents.[2]

Fluoride is widely incorporated into dentifrices as a fundamental component of caries prevention. When cariogenic bacteria produce organic acids, fluoride diffuses alongside them into the dental surface, where it is incorporated into the apatite lattice, thereby inhibiting demineralization.[3] This mechanism preserves the mineral content of dental tissues while simultaneously enhancing remineralization. Saliva, which is supersaturated with calcium and phosphate ions, plays a critical role in this process; as fluoride integrates into the apatite lattice, it attracts these ions toward the tooth surface, forming a fluoride-rich layer that reinforces enamel architecture and increases resistance to acid challenges.[3]

The application of nanohydroxyapatite (nano-HA) in dentistry represents an emerging and promising field. Enamel and dentin are naturally composed of approximately 90% and 60% hydroxyapatite by weight, respectively. Nano-HA was originally developed in the 1970s following observations by NASA as astronauts experienced significant mineral loss and increased dental caries during space missions. Since then, nano-HA has been incorporated into various oral care products, demonstrating significant remineralization benefits.[4] Due to their reduced particle size (approximately 20–100 nm), nano-HA particles can penetrate enamel microporosities and dentinal tubules, promoting effective mineral restoration.[4] In contrast, conventional hydroxyapatite dentifrices contain microparticles (approximately 5–10 μm) that are considerably larger than enamel crystals; this disparity limits their integration into the tooth structure, thereby reducing their effectiveness in remineralization and the management of dentin hypersensitivity.[4]

Biocompatibility studies have consistently shown that nano-HA integrates with mineralized tissues without inducing toxicity or inflammatory responses.[5] This integration occurs through the formation of chemical bonds that facilitate superior adhesion and integration into bone and dental surfaces. *In vitro* studies, including micronucleus assays, have demonstrated that nano-HA does not induce genotoxic effects, and its cellular internalization does not appear to disrupt normal cell function. Collectively, this evidence supports the biocompatibility and safety of nano-hydroxyapatite for applications in oral care and preventive dentistry.[5]

Given the fundamental role of fluoride in caries prevention and the burgeoning interest in nanotechnology-based strategies to enhance remineralization and strengthen dental tissues, synthesizing the available evidence on both approaches is essential. Therefore, the present study aims to conduct a narrative review of recent advances in fluoride compounds and nanomaterials−particularly nano-hydroxyapatite−in preventive dentistry, focusing on their mechanisms of action, clinical efficacy, biocompatibility, and potential integration into novel preventive formulations. To ensure a logical and coherent presentation, this review first outlines the fundamental concepts of nanotechnology applied to dentistry, followed by an analysis of nano-enhanced fluoride systems, experimental evidence, and current clinical applications. This structured approach aims to provide an updated and critical perspective to support future research and evidence-based clinical decision-making.

1. Oral Care and Preventive Dentistry

Nano-hydroxyapatite (nano-HA) has been extensively incorporated into oral care products due to its biomimetic properties and high affinity for dental hard tissues. In preventive dentistry, nano-HA promotes enamel remineralization by integrating into demineralized regions and sealing enamel microporosities. Its nanoscale dimensions facilitate penetration into dentinal tubules, resulting in effective tubular occlusion and a subsequent reduction in dentin hypersensitivity. Furthermore, nano-HA has been proposed as a viable alternative or adjunct to fluoride −particularly in patients at risk of fluorosis− owing to its excellent biocompatibility and its lack of interference with amelogenesis.[6]

2. Whitening and Esthetic Effects

In addition to its remineralizing properties, nano-HA has been reported to exert a mild whitening effect. This phenomenon is primarily optical rather than chemical, attributed to the deposition of nano-HA particles onto the enamel surface; this process reduces surface roughness and optimizes light reflectance. Unlike peroxide-based bleaching agents, nano-HA does not induce enamel erosion or exacerbate dentin hypersensitivity, making it a safe candidate for long-term integration into daily oral hygiene regimens.[7]

3. Nano-HA in Oral Surgery and Bone Regeneration

In oral surgery and regenerative dentistry, nano-HA is widely utilized as a bioactive scaffold for bone grafting and tissue regeneration. Due to its chemical and structural similarity to the natural bone mineral, nano-HA exhibits significant osteoconductive properties and promotes osseointegration when applied in bone grafts, periodontal defects, and implant surface coatings. These characteristics underscore its clinical utility in maxillofacial surgery and implant dentistry.[8]

4. Concentrations and Presentations in Dental Products

The clinical performance of nano-HA is strictly dependent on its concentration and delivery system. Dentifrices designed for daily hygiene typically incorporate 5–10% nano-HA, a range demonstrated to be effective for enamel remineralization and surface protection. Alternatively, high-performance formulations may utilize lower concentrations (1–3%) combined with optimized nanoparticle dispersion to achieve equivalent clinical outcomes. For therapeutic applications, such as the management of acute dentin hypersensitivity or professional-use systems, concentrations of up to 15% have been reported. In mouthwashes, nano-HA is utilized at significantly lower levels, with concentrations up to 0.465% classified as safe according to current consumer safety assessments.[9]

5. Nanotechnology: Fundamentals in Dentistry

Nanoparticles are formally defined as structures with at least one dimension within the 1 to 100 nanometers (nm) range, where 1 nm is equivalent to one billionth of a meter (1 nm = 10^{-9} m). While this definition is widely accepted within the scientific community, certain regulatory bodies and international organizations −such as the ISO or the FDA− may introduce slight variations regarding the precise thresholds of this scale. It is worth noting that nanoparticles can occur naturally −as observed in volcanic ash, sea spray, or fine mineral dust− but can also be engineered through nanomanufacturing processes to meet specific functional requirements or clinical applications.[10]

In recent years, the use of nanotechnology in dental materials has primarily aimed to enhance their mechanical properties, increase wear resistance, reduce polymerization shrinkage, and improve both optical characteristics and esthetic appearance. Currently, nanoparticles are known to exhibit a variety of valuable properties, including bioactivity and antimicrobial effects. Although multiple studies report improvements in mechanical properties and antimicrobial activity following nanoparticle incorporation, these benefits are not consistently observed across all dental materials. Differences in particle size, surface modification, and concentration appear to largely explain the heterogeneous outcomes reported in the literature. Therefore, while nanotechnology offers promising advantages, its clinical effectiveness remains highly dependent on material formulation and the specific application context.[11-13]

Within dentistry, and particularly in endodontics, nanoparticles are applied in tissue regeneration and controlled drug delivery. The ultimate goal is to optimize oral health, with the elimination of biofilms and microorganisms through nanoparticles being a primary focus of current research. These characteristics improve the functionality of dental materials, increase their mechanical strength, provide bioactivity, and enhance antimicrobial effects factors that are essential within the oral environment.[13]

Biofilm is an organized community of microorganisms embedded in a protective extracellular matrix, which grants it high resistance to traditional treatments. Its presence is associated with the development of dental caries, periodontal disease, and persistent infections. Due to their reduced size and high surface-to-volume ratio, nanoparticles can penetrate this matrix and more effectively facilitate its disruption.[14]

Additionally, the protein corona forms when nanoparticles enter a biological environment and become coated with proteins present in that medium. This adsorbed layer alters their physicochemical surface properties and determines their interaction with cells, tissues, and the immune system, directly influencing their biocompatibility and therapeutic performance.[12]

6. Nanotechnology-Enhanced Fluoride

To address the limited adhesive capacity of glass ionomers and the lack of fluoride release in conventional resin-based sealants, fluoride-enriched resin sealants have been developed. Several antibacterial nanofillers, including ZnO, Ag, and TiO_2 nanoparticles, have been incorporated into dental materials; however, their clinical applicability differs substantially. While silver nanoparticles (AgNPs) have shown a favorable balance between antimicrobial efficacy and material compatibility, ZnO and TiO_2 nanoparticles have raised concerns due to reported cytotoxic effects, which may limit their translational potential despite promising antibacterial activity.[14]

Graphene, in turn, is a two-dimensional nanomaterial composed of carbon atoms arranged in a hexagonal honeycomb lattice. Owing to its exceptional properties −including remarkable antimicrobial activity, superior mechanical characteristics, high chemical stability, and notable compressive strength− it has attracted considerable interest in recent dental research. Furthermore, its outstanding biocompatibility and advantageous tribological behavior make it a promising candidate for enhancing the performance of various dental biomaterials.[13]

Fluorinated graphene oxide (FGO) is a derivative of graphene, characterized by a monolayer-thick structure that exhibits exceptional properties. However, research concerning FGO is still in its infancy; consequently, a limited number of studies have been published regarding its applications, particularly within the biomedical field and its capacity for fluoride loading and release.[14]

The incorporation of silver nanoparticles (AgNPs) into glass ionomer cement (GIC) powder can inhibit biofilm formation without significantly affecting its physical and mechanical properties. It has been reported that silver nanoparticles do not strongly integrate with the matrix; consequently, they do not substantially enhance the mechanical properties of the material, possibly due to their nanoscale size, which allows them to disperse among the polymeric chains.[15]

In addition to releasing fluoride into the oral environment upon contact with saliva, GICs can be recharged via fluoride-containing dental gels or mouthwashes. However, there is limited information in the literature regarding the fluoride absorption and recharge capacity of glass ionomers reinforced with silver nanoparticles. The rechargeable nature of glass ionomer cement is likely due to its capacity to sequester and subsequently re-release ions from a solution, acting as a "rechargeable reservoir" for various ions, including fluoride. Consequently, most studies on fluoride ion uptake have assessed ion concentrations in the solutions through analyses performed before and after GIC immersion (see Table 1).[15]

Table 1. *Nanoparticles Applied in Preventive Dentistry and Their Main Effects*[10-15]

Type of nanoparticle	Dental material / Vehicle	Main mechanism	Type of evidence
Nano-hydroxyapatite (nano-HA)	Dentifrices, sealants, varnishes	Enamel and dentin remineralization; reduction of dentin hypersensitivity	*In vitro* / Clinical trials
Silver nanoparticles (AgNPs)	Glass ionomer cement (GIC), silver diamine fluoride (SDF)	Antibacterial activity; biofilm inhibition	*In vitro*
Selenium nanoparticles (SeNPs)	Silver diamine fluoride (SDF)	Enhanced antibacterial activity with acceptable biocompatibility	*In vitro*
Graphene / fluorinated graphene nanoparticles	Sealants and resin-based materials	Antibacterial activity; improved mechanical properties; fluoride release	*In vitro*
Indium oxide nanoparticles (In_2O_3)	Colloidal solutions	Enamel remineralization	*In vitro*
Seashell-derived nanoparticles	Glass ionomer cement (GIC)	Improved mechanical properties and fluoride release	*In vitro*

7. Evidence of Effectiveness

The incorporation of nanoparticles into preventive materials has significantly enhanced the clinical performance of glass ionomer cements. A recent *in vitro* study demonstrated that the addition of seashell-derived nanoparticles to GIC markedly improved both its mechanical properties and fluoride release. Formulations containing 5% and 10% nanoparticles demonstrated significant increases in compressive strength and microhardness, with the 10% concentration yielding the greatest effect. These formulations also exhibited higher fluoride release than conventional GICs, suggesting enhanced preventive potential due to increased fluoride availability in the oral environment. These findings support the use of bioactive nanofillers as a promising strategy to bolster the effectiveness of preventive materials and reduce caries risk.[15]

The remineralizing efficacy of indium oxide (In_2O_3) nanoparticles was evaluated in comparison with sodium fluoride and deionized water. Characterization and analysis were conducted using scanning electron microscopy (SEM), energy-dispersive X-ray spectroscopy (EDX), and X-ray diffraction (XRD). The authors demonstrated that the application of nanoparticles obtained via laser ablation induced significant modifications in the chemical composition and ultrastructure of enamel. Both preventive and therapeutic groups exhibited improvements in enamel remineralization following nanoparticles treatment, with results comparable −and in some instances, superior− to those achieved with fluoride. These findings suggest that colloidal suspensions of indium oxide may serve as an effective alternative to conventional fluoride mouthwashes.[16]

The incorporation of selenium nanoparticles (SeNPs) into Silver Diamine Fluoride (SDF) restorative material has been shown to significantly enhance its antibacterial efficacy against critical oral pathogens, including *Enterococcus faecalis, Lactobacillus, and Streptococcus*. In an *in vitro* study, three SDF formulations containing SeNPs (3%, 4%, and 5%) were evaluated and compared with conventional SDF. The 5% concentration produced the largest zone of inhibition while maintaining cell viability within acceptable ranges. These findings suggest that combining SDF with SeNPs may potentiate the preventive and therapeutic effects of fluoride, offering a promising strategy for controlling cariogenic activity in coronal and root caries without compromising material biocompatibility.[17]

8. Current Clinical Applications

• Use in Children

A randomized clinical trial conducted in 2025 involving children aged 5 to 9 years evaluated the efficacy of 38% silver diamine fluoride (SDF) compared to 5% sodium fluoride (NaF) varnish for arresting interproximal caries in primary molars. After a 12-month follow-up period, SDF showed a significantly higher caries arrest rate (76.3%) compared to NaF (47.3%), particularly in lesions extending into the dentin. These findings suggest that SDF represents a more effective alternative for the prevention and control of caries in primary teeth. This supports its clinical implementation in pediatric dentistry as a highly efficient preventive strategy.[18]

Juárez López *et al.*[19] conducted a randomized clinical trial assessing the effectiveness of photobiomodulation (PBM) combined with an autocured glass ionomer sealant in children aged 6 to 12 years with molar incisor hypomineralization (MIH). The intervention significantly reduced hypersensitivity, improved oral hygiene, and increased sealant retention compared to sealant application alone. After a 30-day follow-up, 56.5% of teeth treated with PBM exhibited complete sealant retention, compared to 17.4% in the control group. These findings demonstrate that combining PBM with glass ionomer sealants is an effective and contemporary clinical strategy for the preventive management of MIH-affected teeth in pediatric populations.[19]

Flynn *et al.*[20] compared the efficacy of CPP-ACP MI Varnish and ProSeal sealant in preventing white spot lesions (WSLs) in adolescent orthodontic patients (12–17 years) over 12 months of fixed appliance treatment. Results indicated that both products provided similar levels of protection against WSL formation, although lateral incisors and gingival areas showed greater susceptibility. Poor oral hygiene was associated with an increased risk of decalcification. This study supports the clinical use of calcium-phosphate varnishes and resin sealants as effective strategies for preventing early lesions in orthodontic patients, emphasizing the importance of combining preventive products with oral hygiene education.[20]

• Use in adults

The efficacy of 5% fluoride varnish, low-level laser therapy (LLLT), and their combination was compared in adults with dentin hypersensitivity using a split-mouth design with a 6-month follow-up period. All treatment modalities significantly reduced hypersensitivity compared to baseline; however, the combination of fluoride varnish and LLLT showed the greatest reduction and the most sustained effect. These results highlight that integrating fluoride varnishes with modern adjuvant therapies can improve the clinical management of dentin hypersensitivity in adult patients.[14]

The efficacy of fluoride varnish, Sylc® bioactive glass powder, as well as a light-cured desensitizer (SHIELD FORCE PLUS) was also evaluated in adults with dentin hypersensitivity associated with non-carious cervical lesions (NCCLs). After six months of follow-up, the light-cured desensitizer provided rapid and sustained relief, while the fluoride varnish, although effective, demonstrated lower reliability when applied as a single dose. These findings suggest that modern desensitizers and fluoride varnishes remain relevant and effective tools for the clinical management of dentin hypersensitivity in adult patients.[15]

The effects of fluoride varnish, xylitol varnish, and their combination on biofilm and saliva in 120 patients with fixed orthodontic appliances showed that fluoride varnish and the fluoride/xylitol combination significantly reduced *Streptococcus mutans* colonies in saliva and dental biofilm. These treatments were found to be more effective than xylitol varnish alone. No significant differences were observed between fluoride varnish and the fluoride/xylitol combination, supporting the clinical efficacy of fluoride in caries prevention in orthodontic patients and suggesting that the addition of xylitol does not provide an additional advantage in reducing cariogenic bacteria.[16]

9. Advantages and Limitations

The incorporation of nanotechnology into preventive dentistry has demonstrated significant clinical benefits, notably the enhancement of the mechanical properties of dental materials, improved wear resistance, increased bioactivity, and antimicrobial effects against oral biofilms. Glass ionomer and resin-based sealants enriched with silver nanoparticles, graphene, or seashell-derived particles have shown increased fluoride release and recharge, contributing to improved caries prevention. Additionally, nanoparticles such as indium oxide and selenium have demonstrated remineralizing and antibacterial efficacy, offering promising alternatives to traditional treatments.[17]

In pediatric populations, clinical trials have confirmed the effectiveness of 38% SDF and the combined use of photobiomodulation (PBM) with glass ionomer sealants in caries control and the reduction of hypersensitivity. In adults, fluoride varnishes, low-level laser therapy (LLLT), and light-cured desensitizing agents have shown efficacy in managing dentin hypersensitivity and reducing biofilm accumulation, including in patients with fixed orthodontic appliances.[11-16]

However, several limitations remain. Some materials may exhibit cytotoxicity (e.g., ZnO, TiO_2), and evidence regarding fluoride recharge in certain materials remains limited. Clinical research on fluorinated graphene derivatives and emerging nanoparticles is also insufficient. Further *in vivo* research and long-term clinical trials are required to validate the safety and effectiveness of these innovations.[18]

CONCLUSIONS

In conclusion, integrating nanotechnology into preventive and restorative dentistry is a promising strategy to enhance clinical treatment outcomes. The incorporation of nanoparticles into materials such as glass ionomer cements, resin sealants, and silver diamine fluoride has been shown to improve mechanical properties, increase fluoride release and recharge, enhance antibacterial activity, and promote remineralization of enamel and dentin. Clinical studies in both pediatric and adult populations support the effectiveness of these innovations in caries prevention, dentin hypersensitivity management, and biofilm reduction, with results comparable or superior to those of conventional treatments.

Nevertheless, certain nanoparticles may present cytotoxicity, and the evidence regarding emerging derivatives and their long-term behavior remains limited. Additional research is required to ensure safety and to optimize their clinical application.

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