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localized application of nanoparticles for dental caries therapy.

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ABSTRACT

The benefits of local drug delivery for tooth caries include targeted therapy and fewer side effects. The use of nanotechnology in this field has become more popular during the past several years. This literature search has produced a succinct summary of the latest advancements in the application of nanoparticles for local therapy for dental caries. When used as delivery systems, nanoparticles can trap medications and other compounds and benefit from their small size and improved penetration. They can also benefit from biomimetic techniques to deliver better care. Comprehensively, in situ dental caries therapy with nanotechnology may bring a new dental tool.

Keywords
Dental caries, Nanotechnology, Biomimetic, Drug delivery, Dentistry

INTRODUCTION

After trauma, dental issues are the second most common cause of acquired disorders in the oral cavity, which is the first part of the gastrointestinal system to be injured. The on-site care acts as a minimizes unwanted effects while providing tailored therapy in the affected area [1,2].

Dental caries, also known as tooth decay, is one of the most prevalent diseases in humans and is characterized by acidic byproducts from the bacterial fermentation of food carbohydrates that can cause localized damage to dental hard tissues [3]. This issue is caused by bacteria that ferment carbohydrates, which demineralizes dental enamel and forms cavities. This process results in the formation of acid. Supplementing with calcium and phosphate can lessen tooth demineralization and help prevent dental cavities. These ions are also present.whether demineralization or remineralization takes place will depend on their salivary content [4] (Fig. 1).

The most basic anion of fluorine, fluoride, plays a crucial role in among the industrial chemicals. It is a widely used remineralization agent for early dental caries prevention. Topical and systemic forms of fluoride have the ability to react with hydroxyapatite to create fluorapatite or fluoridated hydroxyapatite [4,5].

Because they are patient-acceptable and easy to administer, liquid or semi-solid medicines are the most often used dose forms for dental caries. The primary disadvantage of these forms is their inadequate retention in the oral cavity, which leads to less than ideal treatment outcomes [6].

For many years, toothpaste served as the primary fluoride administration strategy to prevent dental cavities.Furthermore, mouthwashes, gels, and pills have been employed as additional administration structures [7].

The primary barrier preventing their full therapeutic potential is the continuous release of saliva, which weakens and dilutes fluoride-enriched teeth.

Therefore, it appears that fluoride must exist on the surface of the teeth to prevent acid attacks from saliva [4,8].

Recently, there has been a noticeable increase in interest in the use of nanotechnology in dentistry. A family of materials known as nanoparticles has several uses, including the pharmaceutical industry, and particulate physicochemical characteristics. Nanotechnology has revolutionized the efficiency of dental materials, including antimicrobial dental adhesives, dental implants, attractive restorative materials, and denture bases [9–12]. Various kinds of nano-formulations for dentistry and oral health have Researchers have looked into a variety of oral and dental nano-formulations thus far. For local administration in the oral cavity, formulations based on nanoparticles can be combined into a gel or paste or given as an aqueous suspension [13].

This literature review provides a quick overview of the latest advancements in the local treatment of dental caries utilizing nanoparticles.

DENTAL CARIES AND NANOMATERIALS

A family of materials with sizes ranging from 1 to 100 nm, known as nanoparticles, have particulate physicochemical features and a broad variety of uses [14, 15]. Particle characteristics such as hardness, chemical reactivity, and active ingredient

are changed when particle sizes decrease from micrometers to nanometers.

surface area [16]. Nanocarriers are nanoparticles that are employed as a means of transporting another molecule, like a gene or medication. Two frequently utilized nanocarriers are liposomes and micelles. Currently, the use of nanocarriers in dentistry is being investigated, and their special qualities suggest that they may be used in the delivery of antimicrobial agents.

Dental care using nanomaterials can be divided into two primary categories: restorative and preventative [17].

Recent research indicates that nanotechnology, specifically through the regulation of plaque-related biofilms and the remineralization of primary teeth, has produced innovative strategies for the prevention and treatment of dental decay. tooth decay [18, 19].

Even though the oral cavity is home to a wide variety of bacteria, only a few specific species—like Lactobacillus species and Streptococous mutans—are thought to be responsible for tooth decay. Mutans Streptococcus (S. mutans) which are the most prevalent bacteria that host in the oral biofilm were initially discovered by Clarke in 1924 in human caries lesions. But further research by Keyes in 1960 [20] revealed more clear links between this bacteria and dental caries, and it is currently thought to be the primary etiological agent of dental caries in both humans and animals.

In this area, fresh drivers of innovation such as nanotechnological breakthroughs have also proved advantageous. It has been demonstrated that using may promote the intrinsically repaired process of natural biomineralization. nanotechnology. By preventing dental cavities, the use of nanoparticles in toothpaste and other washing solutions has been shown to significantly enhance oral health. Furthermore, nanomaterials used to prevent cavities in dental filling materials and polishing agents.

Dental caries may be prevented by antimicrobial nanoparticles in and of themselves [14, 21].

Dental caries is treated using nanotechnology in two major ways. In the first method, a process known as remineralization uses nanomaterials with the ability to release calcium and fluoride, such as calcium phosphate, calcium fluoride, hydroxyapatite, and fluorohydroxyapatite.

The second strategy involves using antibacterial nanomaterials including zinc oxide nanoparticles, silver, and quaternary ammonium polyethyleneimine [22, 23]. It might also be possible to offer superior results by combining these two strategies. The novel varieties of materials that have been aimed at preventing dental cavities by getting rid of the germs that cause tooth plaque are included below [24].

Particles of nanosilver fluoride

The usefulness of metal ions in lowering bacterial infections has been demonstrated by tens of thousands of studies. Silver (Ag) ions have reportedly demonstrated strong antibacterial action against S. mutans [25]. The exceptional antibacterial activity of metal and metal oxide nanoparticles in the best management of dental caries has been revealed by recent developments.

Ag nanoparticles' antibacterial activity has been proposed to arise through two primary mechanisms: The toxicity of free Ag ions results from the metals dissolving off the surface of these nanoparticles, and the production of reactive oxygen species (ROS) on the surfaces of the nanoparticles causes oxidative stress. [26]. Cell death and metabolic disruption are the results of Ag ions' interaction with the disulfide and sulfidryl groups of enzymes. Additionally, Ag nanoparticles may cause pits in the fragmentation of cells due to bacterial membranes [26–28]. It has been shown that, in comparison to the bigger particles, the smaller Ag nanoparticles had better surface contact with the bacteria and, hence, better antibacterial action.

The information above indicates that certain types of nanosilver-fluoride compounds have already been studied. One of these treatments, nano-silver-diamine-fluoride, has been shown to be effective in preventing dental cavities despite some documented side effects, such as tooth discoloration [28].

For the purpose of preventing dental caries in school-age children who had active caries in their primary teeth, Burns et al. investigated formulations containing nano-silver-fluoride. In permanent teeth, there is no fistula, pulpal exposure, or decay. Using a microbrush, they applied two drops of the prepared formulation (for the test group and two drops of water for the control group) to the tooth for two minutes.

once during a year and a half. After one week, their examination on 130 five-month follow-up teeth in 60 children (mean age of 6.31), revealed no loss. There was a 33.3% test group failure rate and a 65.3% control group failure rate during the 12-month period. The use of an annual nano-silver-fluoride solution, according to the authors, was more effective than a placebo in both strengthening and stopping dentine caries in primary teeth. Additionally, this product outperformed silver diamine fluoride because it lacked a metallic component.neither tasted nor discolored the dental tissue. Additionally, the latter formulation's affordability, ease of synthesis, and independence from clinical settings suggest that it will be useful [29].

Chitosan, nano-silver-fluoride, and other new formulations have presented just now [30].

It has been found that chitosan itself inhibits the growth of S.

Mutans, which is becoming more significant in the prevention of dental decay. For example, chewing gum with chitosan supplementation has been demonstrated to significantly lower oral bacterial counts [31]. Additionally, it can prevent enamel demineralization in vitro by functioning as a barrier against acid penetration [32].

Chitosan is a safe, bioadhesive polysaccharide that aids in tooth binding and enhances medication delivery. Previous reports have indicated that it has natural antibacterial properties as well. But the majority of The stabilizing effect of chitosan on Ag nanoparticles is a major factor in its employment in this composition [32, 33].

Freire et al. examined the cytotoxicity and antibacterial activity of four distinct chitosan, silver, and fluoride nanocomposites in terms of size and form.

The results showed that the formulation on murine macrophages is safer the smaller the particle size. The aforementioned samples' varying sizes and shapes, however, did not result in any appreciable variations in their antibacterial and antifungal properties.

Furthermore, neither the grams negative nor grams positive bacteria's growth curves were affected by the samples. The produced nano-composites, according to the scientists, present an optimistic outlook for the management of multidrug-resistant bacteria and do not pose a significant risk to human well-being [34].

The chitosan nanocomposite not only exhibited no cytotoxic effects but also a lower minimum inhibitory concentration than the silver particles of diamine fluoride. Its potential to reduce dental cavities in youngsters has been clinically investigated [35]. The findings indicate that dental caries can be effectively prevented without leaving any tooth stains.

Invertebrates

Another nanoparticulate method that has been investigated for caries targeted therapy is microgels. Studies have examined the possibility of certain biodegradable materials, such as Pluronic block copolymers, to create micelles with tooth-binding properties and to have antibacterial effects [36].

Chen and colleagues created a polymeric (Pluronic® 123) based micelle system that targets antimicrobial drugs into teeth. The antimicrobial mediator in this system is triclosan, while the tooth binding agents are diphosphoserine and pyrophosphate. The outcomes showed improved affinity for hydroxyapatite (HA) powder as well as prolonged triclosan release in saliva and phosphate buffer over a 24-hour period. They also looked at the binding capacity of the micelle system. in the direction of saliva-pretreated HA discs. Even though there was a competitive binding affinity between the salivary components and micelles during the test, the micelles were still able to slow down the formation of a biofilm. In a test that contributed to oral biofilms, the antibacterial effects were also noted [36]. This test was particularly effective when salivary components were given after brushing to reduce their competitive binding to the dental surface.

In a different study, Chen et al. used Pluronic block copolymers to create a farnesol-containing toothbinding micellar drug delivery system.Alendronate, a biomineral-binding moiety, was employed to accomplish tooth-binding ability. has the capacity to bind to tooth surfaces. Because alendronate may attach to HA crystals, it is superior.

has great affinity and has been employed in clinical settings to treat osteoporosis in the past. In aqueous conditions, pluronic block copolymers have the ability to self-assemble into micelles with hydrophilic shells and a hydrophobic core. As a result, farnesol, a hydrophobic substance, can be enclosed within the micelle's core. This formulation reduces the likelihood of irritations caused by organic solvents, which improves patient compliance. Excellent qualities of this medication additionally include its slow release of the antimicrobial section and its rapid binding to HA.

Additionally, the generated micelles demonstrated a significant suppression of the S. mutans UA159 biofilm on Comparing the untreated blank control micelles to the HA discs. Neither the farnesol-loaded nonbinding micelle nor the farnesol-ethanol solution could effectively ward off S. mutans due to the absence of farnesol retention on the HA disc surface.

creation of biofilms. However, because of their capacity to attach to the HA surface, tooth-binding micelles demonstrated nearly complete biofilm suppression at all dosage levels, even after thorough washing [37].

Their research also used Pluronic copolymers containing triclosan as a model drug and alendronate as the binding agent to synthesize another tooth-binding micelle emulator. The results of the biofilm treatment verified that these tooth-binding micelles inhibited S. mutans UA159's early biofilm formation in comparison to the untreated control. Additionally, the micelles had an impact on the produced biofilm's survivability in a decline when compared to the untreated control biofilm. The produced micelles provided potential anti-biofilm capabilities that could be used in the future, according to the authors.oral disease treatment and prevention [20].

Using biomimetic techniques

Artificial materials, structures, or processes that imitate biological systems or natural processes are called biomimetic

products. Combining the idea of nanotechnology with biomimetic tactics can bring new perspectives and innovative methods to caries prevention and treatment. The organized nanostructure of tooth enamel can be mimicked by combining various biological components, additives, or surfactants with mineral nanoparticles or ion solutions [17].

Current research employs a novel treatment approach: the synthesis of biomimetic tooth enamel using calcium phosphate nanoparticles.The biomineralization of dental hard tissues is largely dependent on the chelating properties of amelogenin and casein phosphopeptide-amorphous calcium phosphate nanocomplexes (CPP-ACP). Furthermore, chitosan has had its chelating and cariogenic qualities investigated [32, 38].

Because CPP-ACP and statherin are comparable in a number of ways, it can stabilize even larger quantities of phosphate and calcium than milk and is hence a salivary biomimetic [39]. An amelogenin-chitosan hydrogel (CS-AMEL) hydrogel for enamel reconstruction to prevent tooth decay and restore erosive lesions was tested by Ruan et al. Because the CS-AMEL hydrogel-repaired enamel had organized bundles of apatite nanocrystals that resembled the structure of enamel, it showed much improved stiffness and elastic modulus than control samples [40]. Zhang et al. claimed in a different study that creating a stable phosphorylated chitosan-ACP nanocomplexes that can replicate the biomineralization process between phosphorylated chitosan and amorphous calcium phosphate (Pchi–ACP) in order to remineralize the enamel sub-surface lesion. Pchi-ACP had a remineralizing impact on dental lesions that was comparable to fluoride. According to their research, Pchi–ACP treatment had a much higher rate of mineralization than fluoride treatment [38]. Another has also been reported by Nguyen et al.

Nanosized liposomes are used in a biomimetic strategy. The vesicular nanostructures' biomimetic function mimics the acquired enamel pellicle, which causes salivary proteins to selectively adsorb onto enamel surfaces, sparing the dental enamel's physical barrier of protection.

More research is necessary before using this liposome in clinical training, though. Liposomes coated with pectin did not congregate in a salivary milieu. This makes them potentially useful drug delivery systems for use in the oral cavity. Dental enamel surfaces and HA were both suitable surfaces for pectin-coated liposomes to bind to. Uncoated charged liposomes and pectin-coated liposomes were both able to stay on the enamel surfaces under light shear stresses [41].

Furthermore, tooth stability may be increased and enamel erosions might be repaired using biomimetic techniques for artificial enamel growth [42]. Numerous lines of evidence demonstrate how well nanotechnology can replicate the in vitro production of nano and/or microstructures during apatite crystallization. One of the most popular strategies in nanotechnology is the application of micelles or micro-emulsions based approaches employing biological surfactants for the synthesis and self-assembly of nanostructures. Generate hydroxyapatite nanorods and modify their surfaces using surfactant monolayers to create unique surface properties that will enable the nanorods to self-assemble into highly ordered enamel prism-like superstructures when Floated up to the water's top. The size and chemical makeup of the artificial hydroxyapatite nanorods are similar to those of natural enamel crystals [43]. This method can be used to replicate how enamel is naturally biomineralized.

Making apatite nanoparticles through the primary extracellular matrix protein, amelogenin, is one of the more promising approaches.

Amelogenin has been employed in many research to promote the establishment of apatite layers that resemble biomimetic enamel and is involved in the formation of natural dental enamel. It enhances the organization and crystallization of apatite [44].

This natural enamel was used by Iijima et al. protein in vitro to regulate the crystallization of calcium and phosphate and to promote the development of rod-shaped apatite nanocrystals. According to their report, the enamel's remineralization surface by the formation of a mineral layer that contains fluoride hydroxyapatite nanocrystals. The creation of tiny rod-like apatite whose habit and orientation were comparable to that of real dental enamel crystals was made possible by the supportive roles played by fluoride and amelogenin in the regulation of habit, size, orientation, and phase of the calcium-phosphate crystals [44].

Reports state that the availability of organic scaffolds and templates is vital to the bioinspired development of structures resembling enamel.

Nonetheless, several publications indicate that even methods for apatite crystallization in natural environments have been proposed without the need of organic scaffolds [45, 46]. Yamagishi and colleagues created an acidic paste made up of of fluoride-hydroxyapatite (F-HAP), which can be applied to treat minor dental decay lesions with minimal loss of native enamel through nanocrystalline development. This formulation forms a smooth coating up to 20 μm thick on the enamel surface in 15 minutes.

Longer nanocrystals that have grown throughout the enamel-paste interface are present in the regrown layer. By fortifying the natural enamel, the F-HAP material can restore enamel without the need for prior excavation. This process not only fixes early caries lesions but also helps to prevent them from recurring. [45]. The biomimetetic techniques based on the use of nanotechnology for enamel synthesis are briefly displayed in Table 1. Additionally, Table 2 included commercialized

nanoparticle compounds for use in dental caries applications.

The restrictions on using nanoparticles

Despite compelling findings from research on the application of nanomaterials in dentistry, there is still much apprehension regarding its biosecurity. Furthermore, there has been an escalating tendency in these issues due to the rising use of nanobiomaterilas, with the high absorption rate being viewed as the primary issue. The unique features of large surface area:volume ratio nanoparticles enable improved absorption through the skin, gastrointestinal tract, and lungs. The build-up of nonbiodegradable nanoparticles in various human organs may cause undesirable consequences in biological tissues. Additionally, According to current research, nanoparticles can position themselves in the central nervous system and breach the blood-brain barrier. Thus, beneath the potentialAn important first step in using nanotechnology for medical applications is to assess the neurotoxic effects of various nanomaterials [47–51].

CONCLUSION

In recent years, several researchers have examined innovative medication delivery strategies and techniques for the local treatment of oral cavity issues. A wide range of substances, such as medications or other chemicals and biomacromolecules, can be delivered to an affected area using nanoparticles.

These nanoscale structures take advantage of their small size, which facilitates simple penetration and allows them to get past bodily barriers.

Additionally, certain nanoparticles can employ biomimetic techniques to form more effective and dynamic pharmacological effects. Even with all of these encouraging data, there is still insufficient clinical use of the previously discussed revolutionary procedures for caries therapy. Based on sophisticated nano-drug delivery, more goods might be offered for sale.strategies in the future.

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