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Technologies and materials of the future for the treatment of oral disorders

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Introduction:

In addition to being one of the most significant factors that put the physical and mental health of the human body in jeopardy, oral disease also places a significant load and strain on both people and society as a whole. According to the most recent definition of oral health that was developed by the World Health Organization (WHO), the data that is currently available appears to indicate that the number of oral diseases that are prevalent in the population is greater than 3.5 billion. Materials, such as filling materials for tooth flaws, osteogenic materials for bone defects, implants for the restoration of missing teeth, and so on, are utilized in the treatment of the majority of oral disorders. Both the dangers of oral diseases and the significance of preserving oral health are gradually becoming more known and respected by the general population, particularly in countries that are still in the process of building their economies. To the best of our knowledge, the global market for titanium dental implants alone had reached $6.3 billion in 2021, according to statistics that are only partially comprehensive. Periodontitis and tooth loss are two examples of oral disorders that have seen an increase in incidence as a result of the aging of the world's population. It is for this reason that the development of oral materials and technologies has enormous opportunities, both in terms of space and social and economic benefits (Dai et al.,2017).

While oral materials have been created for decades, there has been no major progress in the performance of clinically used materials in the past ten years. This is despite the fact that oral materials have been developed. Oral materials that have been used traditionally have a straightforward form and basic purpose. When it comes to filling materials for tooth defects, for example, the primary considerations are bonding and strength properties. Antibacterial and other functions are not taken into account. After the introduction of nanoparticles in the 1970s, the exponential expansion of material science has fostered the iteration of the preclinical sector for oral nanomaterials. This has been the case ever since the introduction of nanomaterials. Materials with at least one dimension in the three-dimensional space at a nanoscale size or that are composed of fundamental components are referred to as nanomaterials. Nanomaterials have been utilized in a variety of disciplines in everyday life, including nano-ceramics, nano-computers, nano-catalytic materials, nano-ceramic materials, and many others. Physical and chemical processes are the primary foundations upon which the technology that is used to produce nanomaterials is currently based. There are a variety of processing technologies that have an impact on the size and mechanism of nanoparticles, which eventually has an effect on the function of nanomaterials. In the field of stomatology, these features assist researchers in better developing the structure, content, and function of oral materials. This helps to compensate for the deficiencies that are present in the conventional treatment of oral disorders and alters the notion of treatment for oral diseases. In particular, the interrelationships that exist between materials and biological organisms are becoming an increasingly important focus for academics. When it comes to the research and development of composite resins, for instance, individuals are no longer consciously pursuing aesthetics and mechanical qualities. Instead, they are paying more attention to the link between materials and oral microbes or soft and hard tissues in the mouth cavity. Furthermore, the nano drug delivery system has the capability to imitate the microenvironment of biological tissues. This allows for the precise distribution of a variety of medications into sick tissues, which ultimately results in an improvement in the usage of drugs (Bernabe et al,2020).

The advancement of manufacturing and technology, in addition to the growth of materials science, has also brought about new potential for the therapeutic treatment of oral disorders. As a result of the emergence, growth, and maturation of the technology behind fifth-generation (5G) mobile networks, it has also been widely utilized in the field of medical, including oral medicine. In addition to being centered on people, 5G is also centered on objects, by which it recognizes the link that exists between and within people and stuff. The application of 5G technology in oral medicine has been shown to be successful at the present time. For example, the problem of delayed and inefficient transmission and retrieval of imaging data has been significantly improved by the introduction of 5G technology, which has also reduced the amount of time that dental patients have to wait for treatment and enhanced the effectiveness of medical professionals. The identification of ozostomia is accomplished through the utilization of wearable devices that are synergized with 5G. Additionally, 5G, when paired with virtual reality (VR) and surgical robots, is utilized for the purpose of remote diagnosis and therapy. Artificial intelligence (AI) has been reported for the inspection of oral tumors according to oral photos; 3D printing technology is used for the preparation of oral biomimetic materials; computer-aided design and computer-aided manufacturing (CAD/CAM) technology has realized the restoration of missing teeth for oral patients in a single visit. These advancements are in addition to the fifth-generation (5G) technology. At the moment, the implementation of cutting-edge technology and manufacturing in the treatment of oral diseases is still in its infancy. In order to facilitate the reform of the therapies for oral diseases, additional integration is required (Hugo et al.,2021).

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Caries :

Dental caries is a disease where bacteria eat away at tooth enamel and other hard dental tissues over time. The World Health Organization has included it in their list of the top three human diseases to prevent and treat, along with cancer and cardiovascular disease; it is one of the most frequent oral disorders. Despite the increased awareness of oral health issues and advancements in dental filling materials, the success rate of caries filling after 5 years is still 50%. This is primarily because filler material development nowadays prioritizes mechanical and aesthetic properties over biological ones. On the other hand, modern anti-caries materials focus more on how they interact with the mouth's microenvironment, particularly the hard tissue's remarkable antibacterial and remineralization capabilities. In this segment, we will go over the basics of anti-carrying nanoparticles, including their principles and tactics (Nakamura et al.,2021).

Antibacteria:

Agonists and AgNPs The positive surface charge of silver ions (Ag^+) is responsible for their antibacterial capabilities; this charge blocks the production of proteins and nucleic acids by microbes via electrostatic action, ultimately leading to their demise. Because of its stability and wide-spectrum antibacterial capabilities, Ag^+ is a key material in fluoride coating that has clinical applications. Unfortunately, oxidation and deposition of Ag^+ on the enamel surface will definitely cause tooth surface coloration when Ag^+ is applied clinically. Oral dysbiosis and systemic toxicity might result from certain toxic reactions caused by a high quantity of Ag^+.

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Silver nanoparticles (AgNPs) are more versatile than conventional Ag+ compounds. One positive aspect is that AgNPs can more easily come into contact with bacteria due to their increased surface area. The antibacterial duration is extended because the smaller particles are able to penetrate dentin and enamel more easily. This provides more evidence that even at low concentrations, AgNPs can exhibit potent antibacterial effects. Interestingly, the study also discovered that applying AgNPs did not cause any noticeable black plaque to build on the teeth. Santos mainly attributed this to the fact that AgNPs do not produce oxides when exposed to oxygen in the mouth (Pimkhaokham,2023).

Several methods for using AgNPs in caries therapy have been devised as the research continues. One example is the use of dual antibacterial agents (MDPB+AgNPs), which provide a stronger antibacterial effect while being biocompatible and having no effect on the strength of the dentin connection. By incorporating reduced graphene into glass ionomer cements (GIC), the antibacterial duration may be successfully extended without compromising the mechanical qualities of the GIC, and the release of AgNPs can be controlled using this substrate. By subjecting AgNPs to specific treatments, it is possible to enhance both their antibacterial and mechanical capabilities. Composite resin materials containing 0.5 wt.% silanized nanofibers (SiO_2/Ag-0.5S) inhibited Streptococcus pyogenes and exhibited satisfactory roughness and bending strength metrics. Compared to Ag+, AgNPs are better at preventing and treating caries, but further trials are still needed to confirm how concentration affects the mechanical qualities of the filling material.

Silver ions and silver nanoparticles Zinc oxide (ZnO) was the material of choice for dental cavities fillings in the late 20th century due to its superior biocompatibility and antibacterial characteristics. Composite resins eventually did away with ZnO adhesives due to their poor mechanical strength and the fact that they interfered with the resin matrix's bonding process. Dentin collagen bundle decomposition can be reduced by inhibiting matrix metalloproteinase (MMP) activity, which can be achieved by adding Zn2+ to the total etching binder. Nanotechnology has revived interest in zinc oxide (ZnO) in the form of zinc oxide particles (ZnNPs), which are better suited to the development of adhesives and filling materials for teeth than micron-sized zinc oxide (Zn2+) (Padovani et al.,2015).

The effect on Streptomyces mutans is substantial when resin materials contain ZnNPs. Just as AgNPs, ZnNPs derive their antibacterial properties from Zn2+. The material's antibacterial characteristics can be impacted by structural modifications as well. The principal antibacterial action of ZnNPs, according to Elena Zanni et al., who created graphene nanoplatelets coated with zinc oxide nanorods, is not the generation of reactive oxygen species (ROS) but rather the related mechanical damage to the cell surface of this oral pathogen. These findings highlight the multi-functional antimicrobial properties of ZnNPs. In light of this finding, Wang et al. transformed Ag+ into ZnO nanorods. Through surface potential and oxidative stress reactions, they discovered that this material could physically harm bacteria to a point where it killed them. To make plaque removal even more successful while brushing, scientists have recently developed an antibacterial toothbrush that uses AgNPs and ZnNPs. However, whether or not this toothbrush may cause oral microbes to acquire antibiotic resistance is unknown because long-term test findings are lacking.

Consequently, it is a valid concern to think about how to employ antibacterial nanomaterial methods without causing a dysbiosis of the oral flora (Bastos et al.,2021).

antibiotics that react with changes in pH There have been other attempts at using metal ions as antibacterial agents, in addition to the two conventional anti-caries compounds listed above. These metal ions work mostly in the same way to inhibit bacterial growth, but they are poisonous and hence difficult to include directly into filler materials. We won't bore you with the specifics of these materials here.

The acidification of the extracellular polysaccharide matrix is associated with cariogenic biofilm. As a result, there has been a recent push to produce pH-responsive anti-caries materials, which can enhance drug targeting. For instance, in 2015, exopolysaccharides, saliva-coated hydroxyapatite (sHA), and positively charged nanoparticles were created. This substance uses its positive surface charge to specifically target bacterial biofilms. The nanomaterial's structural stability will be compromised in acidic settings, leading to the release of the hydrophobic substance farnesol, which has antibacterial properties (Bicak ,2021).

The DEX-NZM coating, which is made of dextran iron oxide, is another substance that responds to changes in pH. Although iron oxide nanozymes (NZM) have potent antibacterial effects when stimulating the production of hydrogen peroxide (H2O2) in acidic environments, they are not very stable when dissolved in physiological media and may even harm some healthy tissues. Research has demonstrated that these issues can be effectively addressed by coatings that are made by encasing iron oxide NZM with dextran. Bacterial biofilms are effectively eliminated by this covering. Histopathological examination of gingival tissues could not detect any proliferative

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alterations, inflammatory reactions, necrosis, or other undesirable effects of Dex-NZM, H2O2, or the Dex-NZM/H2O2 combination treatment.

The importance of comprehending the interplay between materials and organisms for rational materials design is shown by these experimental results. But at the moment, antibacterial caries filling materials are the main focus of research and development. Materials such as adhesives, coatings, and dental caries vaccinations could one day be seen in clinical practice, if the design is sensible (Bicak ,2021).

Demineralizaion and remineralization:

items containing calcium dioxide More and more Ca2+-based compounds including HAP, ACP, CaF2, CaSiO4, and others have been produced in recent years to serve as remineralizing agents in medicinal settings. Among these, HAP—which is chemically similar to dentinal tissue—can aid in the remineralization of damaged hard tissues by triggering the production of new bone cells and the release of harmless ions that are involved in metabolism in living organisms. Having said that, HAP isn't ideal for use as a filler material for cavities due to its porous structure and weak mechanical qualities.

The low mechanical characteristics of HAP are mitigated to some degree by nano-hydroxyapatite (NHAP). Early caries involve acid erosion of tooth hard tissues caused by bacterial metabolism, which removes mineral ions but has little effect on the collagen network. To promote remineralization of teeth's hard tissues and prevent caries progression, the porous NHAP can be utilized as both a direct mineral replacement and a carrier of the lost ions in the caries attack. A approach that can penetrate tooth pores and establish a protective layer on the surface of the teeth

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has been studied: adding NHAP to toothpaste. This would give ions that prevent demineralization and increase remineralization. This highlights how Ca^{2+}-based nanomaterials have the ability to remineralize tooth hard tissue (Nakamura et al.,2021).

Contents of phosphates Reducing the demineralization of dental tissues can be achieved by minimizing the loss of PO_4^{3-}, even if PO_4^{3-} is mostly linked to Ca^{2+} to assist in enamel remineralization. Adsorption of sodium trimetaphosphate (TMP) on dental enamel surface decreases demineralization of dental tissue and prevents caries progression by reducing enamel, improving enamel remineralization, decreasing HAP solubility and mineral exchange, and changing the affinity between enamel surface and salivary proteins. Since this polyphosphate is essential for lowering the solubility of HAP, it finds usage as an ingredient in gum and toothpaste formulations. A study found that by adding TMP to low-fluoride toothpaste, the concentration of fluoride was effectively lowered, and the in vitro anti-caries action was comparable to or even better than that of regular toothpaste containing 1100 ppm of F^-. Results like these show that phosphate can act as an anti-caries agent even when no extra Ca^{2+} is present.
In contrast to TMP, nano-trimetaphosphate (NTMP) is able to remineralize in the progressing region, penetrating deep into cavities. A performance test comparing NTMP and TMP shows that NTMP has a far superior remineralization ability when applied alone compared to TMP. Additionally, NTMP makes it easier to release fluoride when added to toothpaste or resin-modified glass ionomer cement (RMGIC) (Pimkhaokham,2023).

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Things made of fluoride F− can displace OH- in HAP and generate fluorapatite, which is more resistant to the acidic environment caused by bacteria, thereby avoiding demineralization of dental tissues, unlike Ca2+ and PO43− direct replenishment techniques for demineralized tissues. Fluoride has been shown to effectively prevent cavities in water and toothpaste for the past few decades. But fluorosis of the teeth and bones can develop from consuming too much fluoride. All of these issues have been adequately addressed by the new nano-fluoride technology. An unstable fluoride reservoir made of one of the nano-calcium fluoride (NCaF2)-based materials can improve the efficacy of fluoride treatment. In the meanwhile, NCaF2 promotes tooth remineralization while simultaneously acting as an agent to reduce dentin permeability. Coating materials containing nano-scale fluoride, particularly those based on silver fluoride, are better able to remineralize antibacterial agents all at once, according to the size effect (Padovani et al.,2015).

Materials for biomimetic remineralization Oral care products containing fluoride and hydrogen apatite (HAP) can stimulate enamel remineralization, however they cannot encourage the creation of ordered apatite crystals. Some have put forward the idea of regenerating hard tissue in teeth as a potential treatment option. In biomimetic remineralization, proteins and inorganic materials interact to produce HAP crystals through an organic matrix. During enamel development, amelogenin can control the creation of organized and highly anisotropic apatite crystals, and synthetic peptides based on amelogenin can accelerate the remineralization of early enamel lesions (Bastos et al.,2021).

the N-terminal amelogenin (N-Ame) with the central domain and the synthetic peptide (C-AMG) based on the C-terminal peptide (C-Ame) with phasetransited lysozyme (PTL) enzyme membrane attached to prevent the polypeptide from being dissolved by saliva. A multifunctional matrix was immobilized with a PTL/C-AMG matrix, which allows C-AMG to support the directed alignment of ACP nanoparticles and their transformation into ordered HAp crystals resembling enamel. PTL serves as a strong interfacial anchor to attach the C-AMG peptide. Nascent HAP was visible on the enamel surface after 7 days of saliva culture, but not on the fluoride surface. Additionally, this highlights the distinction between biomimetic enamel regeneration and remineralization solely caused by fluoride.

The biomimetic mineralization strategies used on enamel and dentin are different because of structural variations. Dentin created through biomimetic remineralization is situated in the lesion body, whereas reparative dentin production begins in the pulp cavity. To reduce primary and secondary cavities and improve dentin bond integrity, demineralizing demineralized dentin is significant. A potential approach that utilizes ACP and non-collagen protein (NCP) analogs to backfill demineralized dentin is the biomimetic remineralization of demineralized dentin utilizing calcium phosphate polymer-induced liquid precursors (Ca/PPILP). This strategy is based on the hypothesis of non-classical crystallization pathways. Bonding strength and interface integrity of remineralized artificial carious dentin lesions can be greatly enhanced using this dentin biomimetic remineralization material (Bicak,2018).

The majority of present methods center on processing filling resin, however both the size effect and the structure effect can greatly enhance the antibacterial characteristics of materials used to prevent caries. We need to pay more attention to more things, but we can dramatically lower the incidence of caries if we can produce more effective caries preventive items like mouthwash, toothbrushes, and toothpaste. The present state of the art in tooth hard tissue remineralization involves two distinct methods: one for enamel and another for dentin. Perhaps, with the help of future technological advancements, we will be able to stimulate the simultaneous regeneration of dental enamel and dentin. Furthermore, 3D printing technology could be utilized to completely recreate the tooth's structure and contour (V. R, 2018).

Dentin hypersensitivity:

Dentin tubules become exposed in the mouth due to abrasion, acid erosion, or trauma. When external stimuli trigger fluid flow in these tubules, pulpal reactive discomfort can result. The main goals in addressing dentin hypersensitivity are to seal the tubules in the dentin and to prevent the transmission of irritation. There are now a variety of desensitizers on the market that can be used to close dentin tubules. Unfortunately, desensitization therapy has only shown temporary results due to the breakdown of most materials in the mouth and low penetration. Alternatively, as dentinal tubules typically have an average diameter of approximately 1-2.5 εm, dental materials that are nano-sized are more likely to be effective in alleviating dentin hypersensitivity (Li et al.,2021).

If you suffer from a dentin allergy, one solution is to use desensitizing toothpaste. A 2% NHAP toothpaste was shown to be effective in a double-blind clinical study by Vano et al. The particle size of NHAP is another component that impacts dentin's capacity to mineralize, in addition to concentration. It is believed that zinc nanoparticles, like calcium nanoparticles, hasten dentin active remodeling, which in turn improves the mechanical characteristics and maturation of dentin. Composite modulus values at intertubular and peritubular dentin were greater following ZnNP treatment compared to CaNP treatment. Dentin hypersensitivity symptoms are alleviated with the use of nanostructured sol-gel bioactive glass (BG) because it decreases the electrical conductivity of acidic solutions. The nano-Si/Ca(Sr) combination has been used to create a material with many functions. An alternative for the present generation of multifunctional nanomaterials, this material can stimulate dentin bionic remineralization while simultaneously being acid resistant, inhibiting bacteria, and having low cytotoxicity (Dananjayan et a.,2021).

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