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Review Paper

A Review on Nanomedicine in Oral Healthcare: Beyond Toothpaste and Mouthwash

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ABSTRACT

Oral diseases are among the most widespread global health problems, and conventional oral care products such as toothpaste and mouthwash often provide limited, short-term benefits. Nanomedicine has emerged as a promising approach in dentistry by enabling targeted, controlled, and efficient delivery of therapeutic agents at the nanoscale. This review highlights recent advancements in nanomedicine for oral healthcare, including the use of metallic nanoparticles, polymeric nanoparticles, liposomes, nanogels, nanohydroxyapatite, and carbon-based nanomaterials. Applications in antimicrobial therapy, periodontal treatment, enamel remineralisation, oral cancer management, diagnostics, and regenerative dentistry are discussed. The review also addresses safety, toxicity, and regulatory challenges associated with dental nanomaterials. Overall, nanomedicine offers a significant shift toward more effective, preventive, and personalised oral healthcare beyond conventional formulations

INTRODUCTION

Oral diseases remain among the most prevalent non-communicable diseases worldwide, posing a significant public health challenge.[1] According to the World Health Organisation (WHO, 2024), nearly 3.5 billion people suffer from oral diseases, with untreated dental caries, severe periodontal disease, tooth loss, and oral cancers being the most common. The global burden is particularly high in low and middle-income countries, where access to oral care, preventive measures, and education remains limited. Poor oral health is closely linked to systemic conditions such as diabetes, cardiovascular disease, and respiratory infections, highlighting the need for more effective and accessible oral healthcare strategies.[2]

Traditional oral healthcare methods, such as toothpaste, mouthwash, and mechanical cleaning, have limitations despite their widespread use.[3]

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These conventional products primarily provide surface-level cleaning and temporary antibacterial action. However, they often fail to deliver therapeutic agents effectively to deeper oral tissues, lack site-specific targeting, and may lead to short-term effects or microbial resistance with prolonged use.[4] Additionally, many formulations contain chemical agents (e.g., alcohol, fluoride, and synthetic surfactants) that may cause irritation, enamel erosion, or altered oral microbiota balance.

In recent years, the rise of nanotechnology in medicine and dentistry has opened new horizons for the prevention, diagnosis, and treatment of oral diseases.[5] Nanomedicine enables the design of materials and carriers at the nanoscale (1–100 nm), allowing enhanced penetration, controlled drug release, bioadhesion, and antimicrobial efficiency within the oral cavity. Nanoparticles, nanogels, nanocomposites, and nano sensors have shown potential in remineralising enamel, managing infections, healing tissues, and delivering drugs to targeted sites. This innovative approach promises to overcome the shortcomings of traditional oral hygiene products.

The scope and purpose of this review are to explore the applications, mechanisms, and advantages of nanotechnology in oral healthcare, moving beyond the limitations of conventional toothpaste and mouthwash. The review aims to discuss current advancements, challenges, safety aspects, and prospects of nanomedicine in improving oral health outcomes, ultimately supporting the transition toward next-generation, personalised, and preventive oral care solutions.

4. Fundamentals of Nanomedicine in Dentistry

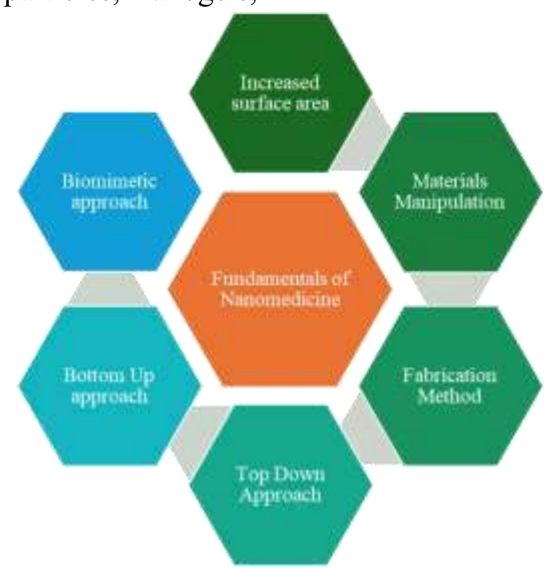

Figure 1: . Fundamentals of Nanomedicine in Dentistry

- Materials Manipulation: Nano dentistry is based upon the capability of engineering and controlling materials at the nanoscale.[6] These materials, called nanomaterials, have unique physical, chemical, and biological properties compared to their bulk counterparts.
- Methods of fabrication: Nanomaterials are fabricated primarily by two methods:
- Top-down approach: This is a process of breaking down larger material into nanostructures; for example, ball milling techniques to produce nanoparticles.

- Bottom-up approach: In this technique, complex structures are built atom by atom or molecule by molecule. It is very precise, and self-assembled nanostructures can also be formed with this technique.[7]
- Biomimetic approach: The working principle is to produce materials that emulate natural dental tissues. Enamel and dentin, being the natural dental tissues, are themselves made up of nanoscale structural units.[8]
- Increased surface area: Nanomaterials have a very high surface area-to-volume ratio, making them more reactive and giving them unique properties. This can be exploited to create better bonding agents, more effective antimicrobial coatings, and superior restorative materials.

4.1 Definition and scope of nanomedicine

Definition: Nanomedicine for oral health can be defined as the application of nanotechnology to diagnose, treat, prevent, and maintain the health of teeth and the mouth. Nanoparticles, nanomaterials, and nanodevices are used in this area to enhance dental care by operating at the molecular and cellular levels.

Scope of Nanomedicine:

Table 1: Scope of Nanomedicine

Scope	Description
1. Preventive Dentistry:	• Nanoparticles are added to toothpaste and mouthwash to prevent plaque, tooth decay, and bacterial growth. • Helps in enamel remineralisation using nano-hydroxyapatite.
2. Restorative Dentistry:	• Nanocomposites improve the strength, polishability, and durability of dental fillings.[9] • Provides better colour matching and longer life of restorations.
3. Periodontal Therapy:	• Nanocarriers deliver anti-inflammatory and antibacterial drugs directly to gum tissues. • Supports regeneration of bone and periodontal ligament using nanofibers and scaffolds.
4. Endodontics (Root Canal Treatment):	• Nanoparticles such as nano silver and chitosan are used for sterilising root canals.[10] • Improves sealing ability and reduces reinfection risk.
5. Implant Dentistry:	• Nano coatings on dental implants enhance osseointegration (bonding with bone). • Prevents bacterial colonisation and implant failure.
6. Oral Diagnostics:	• Nano-biosensors and nanochips detect oral cancer, infections, or systemic diseases through saliva testing. • Enables early diagnosis and personalised treatment.
7. Drug Delivery Systems:	• Nanoparticles help in the controlled and targeted release of drugs in the oral cavity. • Reduces side effects and increases therapeutic efficiency.

4.2 Nanoparticles and nanoscale systems :

Types of nanoparticles and nanoscale systems

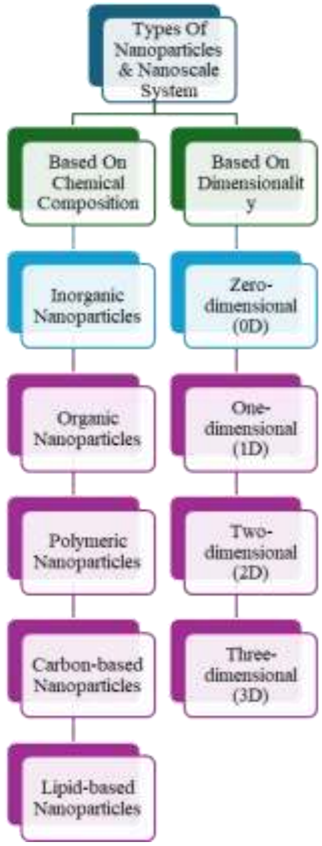

Figure 2: Types of nanoparticles and nanoscale systems

- **Biocompatibility**

Surface functionalization is all about tweaking the surface of nanoparticles to make them work better and fit into biological systems. When you add polyethene glycol (PEG) to the surface, a process called PEGylation, you boost how long the nanoparticles stay in circulation and make it harder for the immune system to spot and remove them. You can also attach antibodies or other ligands to direct the nanoparticles to specific cells or tissues, which helps cut down on hitting the wrong targets. Using materials that break down over time, like certain polymers and organic compounds, means the nanoparticles don't stick around and cause trouble later.[11] That takes care of a lot of the long-term toxicity issues, since the body clears them out naturally. Still, nanoparticles, especially those made from inorganic materials or heavy metals, can be reactive and sometimes risky. That's why surface modifications aren't just helpful; they're necessary to keep potential toxicity in check

- **Material compatibility**

You can mix nanoparticles into bigger materials, like polymers, to make nanocomposites that are stronger or better at handling heat and blocking gases. But here's the catch: nanoparticles have high surface energy, so they tend to clump together. When that happens, you lose the special properties you want. That's why it's important to make sure they mix well and stay evenly spread out in the material.

There's also the option to blend different kinds of nanoparticles, say, organic and inorganic, to build hybrid systems that work even better together. Take coating a metal core with a polymer, for instance. That move helps you get the stability of the metal, but with the bonus of biocompatibility from the polymer.[12]

4.3 Advantages of conventional therapies:

Advantages of targeted drug delivery over conventional therapy

Improves bioavailability

Targeted drug delivery fixes a bunch of problems that make regular drugs less effective. Here's how it works:

- Encapsulation: A lot of these systems rely on tiny carriers like nanoparticles, liposomes, or polymeric micelles—to wrap up the drug. This shield keeps the drug safe from getting broken down by stomach acid or liver enzymes, something that happens a lot with pills.[13]
- Better solubility: These carriers also boost how well a drug dissolves, which is a big deal for drugs that don't mix well with water. Thanks to their small size and big surface area, nanoparticles help the drug dissolve more easily in the body, so it gets absorbed better.
- Skipping first-pass metabolism: Because targeted delivery sends the drug right where it's needed, it dodges the liver's first-pass effect, which is when the liver breaks down drugs before they can really do their job.
- Longer circulation: Scientists can tweak these carriers by adding things like polyethene glycol (PEG). That way, the immune system ignores them, letting the drug hang around in the bloodstream longer and giving it a better shot at hitting its target.

Reduces side effects

Targeted delivery stands out because it really helps cut down on side effects.[14] Here's how it works. First, it keeps most of the drug right where it's needed, at the diseased area, instead of sending it all over your body. So, healthy organs and tissues get exposed to a lot less, which means they're less likely to get hurt in the process.[15]

Another upside you don't need as much of the drug overall. Since more of it reaches the exact spot where it's supposed to act, doctors can use a lower dose to get the same result. That cuts down the chances of the drug causing problems in the rest of your body.

And when it comes to harsh treatments, like chemotherapy, this approach can make a huge difference. Chemo drugs are powerful, but they also hit healthy cells, which leads to things like hair loss, nausea, and a weaker immune system. With targeted delivery, doctors can spare a lot of those healthy cells. Take liposomal doxorubicin, for example, which collects tumours much more than in the heart, so patients have a much lower risk of heart damage compared to regular doxorubicin.

Mechanisms for improving targeted delivery

Targeted delivery systems use a mix of strategies to get drugs exactly where they're needed.

With passive targeting, the system takes advantage of how the body works, especially the way tumours usually have leaky blood vessels and lousy lymphatic drainage. Because of this, nanocarriers tend to build up and stick around in tumour tissue more than in healthy areas.[16]

Active targeting goes a step further. Here, scientists attach things like ligands, antibodies, or peptides to the drug carriers. These "address labels" home in on specific receptors found in high numbers on target cells, making the delivery much more precise.

Then there's stimuli-responsive delivery. In this case, nanocarriers only release their cargo when they hit certain triggers like a particular pH, a change in temperature, or the presence of certain enzymes. Sometimes, it's even something from outside the body, like a magnetic field or a burst of ultrasound, that sets things off. This way, the drug stays put until it reaches the right spot.

5. Types of Nanomaterials Used in Oral Healthcare

Nanoparticles are changing the way we approach oral hygiene. You'll find silver nanoparticles, hydroxyapatite, and silica popping up in all sorts of dental products these days. Dentists use them to make stronger fillings, coat implants with nanostructured surfaces, and fight off bacteria that cause cavities and infections. There are others in the mix too, like carbon nanotubes, zirconia, titania, and iron oxide. All these materials help push dental care forward.[17]

Common types of nanomaterials:

Table 2: Common types of nanomaterials

Types Of Nanoparticles	Description
Silver nanoparticles	Used for their strong antibacterial properties in materials like denture bases and to treat infections.
Hydroxyapatite (HAp)	A key component of natural teeth and bone, it is used to remineralize enamel and improve biocompatibility.
Nanocomposites	Mixtures of nanoparticles (like glass, alumina, or silica) and polymers used in dental fillings, sealants, and restorative materials to improve strength, durability, and aesthetics.
Ceramics	Materials like zirconia and titania are used for dental restorations, implants, and prosthetics due to their strength, hardness, and tooth-like color.
Carbon nanotubes	Added to composites and other materials to improve mechanical properties and durability.
Silica	Used to enhance mechanical properties in products like nanocomposites and in coatings for dental implants.

5.1 Metallic nanoparticles (silver, gold, zinc oxide) – antimicrobial & anti-inflammatory

Metallic nanoparticles like silver, gold, and zinc oxide (ZnO) pack a serious punch against microbes and inflammation, each working in its own way. Thanks to their tiny size and big surface area, they show a lot of promise for treating infections and inflammatory conditions. Still, there are real worries about how toxic they might be to human cells and what could happen over time. A lot depends on their size, shape, how much you use them, and what's on their surface.[18]

1. Silver nanoparticles (AgNPs)

AgNPs are potent, broad-spectrum antimicrobial agents that have been used for centuries and are effective against bacteria, fungi, and viruses, including many multidrug-resistant strains. AgNPs also possess anti-inflammatory properties, which can help promote wound healing.

- **Antimicrobial mechanisms**

First, AgNPs attack the cell wall and membrane. They stick to the surface, mess up the structure, and make the membrane leaky. Stuff from inside the cell starts spilling out.

Then, AgNPs ramp up the production of reactive oxygen species, basically, toxic molecules that stress out the bacteria. These ROS tear into cell parts like lipids, proteins, and even DNA.

Smaller AgNPs go a step further. They slip inside the cell and latch onto molecules that contain sulfur and phosphorus, including DNA and key proteins. This messes with vital processes like DNA replication and protein synthesis.

On top of all that, AgNPs can knock out some of the bacteria's defenses, making them easier targets for regular antibiotics. So, they hit bacteria from several angles at once.[19]

- **Anti-inflammatory mechanisms**

AgNPs step in and dial down pro-inflammatory cytokines like TNF-α and IL-1β, while giving a boost to the ones that calm things down. They also lower VEGF levels by shutting off certain signaling pathways, which helps keep blood vessels from getting too leaky during inflammation. On top of that, research shows AgNPs can block the COX-2 enzyme pathway, a key player in ramping up inflammation.

2. Gold nanoparticles (AuNPs)

People usually see AuNPs as more biocompatible than AgNPs. Researchers have developed them as antimicrobial agents, often tweaking or functionalizing them to boost their impact. Besides that, AuNPs show anti-inflammatory effects by changing how cells communicate and signal each other.

- **Antimicrobial mechanisms**

Gold nanoparticles (AuNPs) on their own don't do much to bacteria, but once you coat them with the right molecules like antibiotics, peptides, or certain ligands, they become way more effective at killing germs.[20] There's also the photothermal effect. If you use nanorods or nanoshells and hit them with near-infrared light, they heat up and destroy bacteria by basically cooking them, but without frying the healthy tissue nearby. Some AuNPs, especially the ones with a positive charge, mess with bacterial membranes. They stick to the membrane, break it apart, and that's the end for the bacteria. And then there's their knack for blocking protein synthesis; they get in the way of tRNA binding at the ribosome, so the bacteria can't build the proteins they need to survive.

- **Anti-inflammatory mechanisms**

AuNPs step in as oxygen radical scavengers, cutting down the amount of ROS that phagocytes produce, the same cells that kick off inflammation in your body. They also dial back the production of pro-inflammatory cytokines, like IL-1β and TNF-α, so these molecules can't stir up as much trouble. Plus, AuNPs tweak signaling in immune cells like macrophages (including Kupffer cells), especially in pathways like MAPK and PI3K. These pathways play a big role in how inflammation gets regulated.[21]

3. Zinc oxide nanoparticles (ZnO NPs)

ZnO NPs pack a punch when it comes to fighting off bacteria and fungi, and they don't break the bank either. On top of that, they help calm inflammation and speed up wound healing.

- **Antimicrobial mechanisms**

ZnO nanoparticles fight microbes in a few key ways. First, they crank out reactive oxygen species, basically, tiny chemical bullies that attack and damage the cells by causing oxidative stress.[22] This messes with the microbes' insides and leads to cellular damage. On top of that, ZnO nanoparticles can break up the cell membrane, poking holes or even rupturing it. When that happens, the cell's contents leak out, and the microbe dies. There's also the release of zinc ions. Once ZnO dissolves, these ions flood out, messing with import.[23]

- **Anti-inflammatory mechanisms**

ZnO NPs work against inflammation in a few ways. First, they shut down the production of pro-inflammatory cytokines like TNF-α and IL-1β, so the overall inflammatory response drops. They also get in the way of the NF-κB pathway, blocking the genes that drive inflammation by keeping the p65 protein out of the cell nucleus. On top of that, ZnO NPs lower COX-2 enzyme levels, which cuts down on inflammatory mediators.

They even knock back iNOS expression, which means less nitric oxide (NO) gets made. Since NO is toxic and ramps up inflammation, reducing it helps calm things down, and the effect gets stronger with higher doses.

5.2 Polymeric nanoparticles – sustained release for oral drugs

Polymeric nanoparticles aren't just for toothpaste or mouthwash; they're changing how we deliver drugs by mouth in all sorts of medical treatments. When you wrap a drug in a polymer shell, it gets a kind of armour that shields it from the tough conditions inside your gut. Plus, these nanoparticles let you control exactly how fast the medicine gets released, which makes the whole process a lot more efficient.

- **Oral delivery of biologics**

A lot of biologic drugs, proteins, peptides, and nucleic acids don't survive the harsh environment of the stomach. Acids and enzymes break them down, and even if they make it through, the intestine doesn't absorb them well. Polymeric nanoparticles step in here. They shield these sensitive drugs, so instead of needles and expensive injections, people can just take a pill.

Take diabetes, for example. Scientists have spent years chasing oral insulin. Polymeric nanoparticles have made real progress here.[24] They built a delivery system that senses pH changes, so it holds onto insulin in the stomach's acidic soup and only releases it once it hits the small intestine.

Inflammatory bowel disease is another case. Researchers designed nanoparticles to carry anti-inflammatory drugs or even gene therapies like siRNA straight to the inflamed spots in the gut. These particles are smart; they're built to respond to spikes in reactive oxygen species, the chemical markers of inflammation, so they drop their payload exactly where it's needed.

- **Cancer treatment**

Polymeric nanoparticles give oral cancer treatments a real boost. They help keep the drug working longer, target the right spot, and make the medicine more effective so you get more of it where it counts and fewer nasty side effects throughout the body.[25]

When it comes to chemotherapy, wrapping the drugs inside these nanoparticles makes them hit cancer cells harder. Plus, they help tackle that tricky problem of multidrug resistance, where cancer starts ignoring regular treatments.

You can also tweak these nanoparticles to home in on cancer cells. Scientists attach special molecules to their surfaces, so they stick almost exclusively to tumors. That way, the drug piles up where it's needed most and doesn't bother healthy tissue as much.

There's more. These nanoparticles can double as both medicine and a way to monitor how things are going. By combining a therapy with an imaging agent in the same nanoparticle, doctors can treat the cancer and track its progress at the same time.

- **Remineralisation and repair**

Beyond just making teeth look better, polymeric nanoparticles play a big role in advanced oral repair and regenerative medicine.[26] Take enamel and dentin remineralisation, for example. Researchers use nanoparticles made from calcium phosphate, things like amorphous calcium phosphate (ACP), to target spots where enamel or dentin has lost minerals. Polymers such as polyacrylic acid help keep the ACP stable and let it release slowly, which really boosts remineralisation.

Then there's bone regeneration. In tough cases, like fixing major jawbone damage, polymeric nanoparticles come in handy to deliver growth factors or even stem cells right where they're needed. This approach jumps in to help tissue repair happen faster and more effectively.

○ **Tackling drug absorption barriers**

The GI tract throws plenty of obstacles at oral drug delivery, shifting pH, thick mucus, and fast transit times all get in the way. Polymeric nanoparticles are built to handle these hurdles.

When it comes to mucus, these particles can either stick around on the intestinal lining for a longer stay or they can slip right through to reach the cells underneath. A common trick is to coat them with something neutral and water-loving, like poly (ethylene glycol) (PEG), so they don't get tangled up in the mucus.

For targeting, "smart" polymeric nanoparticles can sense their environment. They only release their drug cargo when they hit the right conditions, like a certain pH or temperature.[27]

And, if you tweak their size, shape, and surface, you can get these nanoparticles to target specific cells, whether it's M-cells in Peyer's patches or straight through enterocytes. This boosts how much of the drug gets absorbed where it's needed.

5.3 Liposomes & niosomes – mucosal adhesion and controlled release

Liposomes and niosomes are tiny vesicles that work as drug carriers in oral health care. They stick better to the mouth's lining and can release medication in a controlled way. Usually, the mouth isn't an easy place for treatments saliva constantly washes things away, enzymes break stuff down, and the lining of the mouth replaces itself fast. That means most topical treatments don't last long. But when you put drugs inside liposomes or niosomes, their bilayer structure protects the medicine and helps it stay where it's needed. This boost lets treatments for oral diseases like cancer, candidiasis, or periodontitis work more effectively.[28]

Liposomes versus niosomes

While both are vesicular nanocarriers, liposomes and niosomes have distinct compositions that impact their stability and cost.

Strategies for mucosal adhesion and controlled release

Liposomes

- Polymer coating: You can coat the surface with mucoadhesive polymers like chitosan, alginate, pectin, or polyethylene glycol (PEG).
- Chitosan: This one sticks well to mucosal surfaces because it bonds with the negatively charged membrane, so the coating hangs on longer.
- PEGylation: When you add PEG, it helps the particles slip through mucus more easily by preventing them from getting tangled up with mucin proteins. That way, they reach deeper into the tissue.
- Targeting ligands: You can tweak the surface of liposomes to target certain cells or receptors in the mouth. Take wheat germ agglutinin (WGA) as an example, it sticks to oral cells, which means better adhesion and more precise drug delivery right where it's needed.
- Stimuli-responsive release: Liposomes aren't just passive carriers. You can design them to release their contents when they hit a trigger, like a drop in pH in inflamed gum tissue, as you see in periodontitis.

Niosomes

- Mucoadhesive buccal films: You can load niosomes into mucoadhesive oral films to keep them in contact with the buccal mucosa longer. Usually, these films use polymers like chitosan, which help control how the niosomes release the drug, so you get a steady, sustained delivery.
- Surface charge modification: When you add charged molecules such as dicetyl phosphate or stearylamine, you change how stable the niosomes are and how they interact with

mucosal surfaces. Niosomes with a positive charge stick better to the negatively charged mucosal surface.

- Biphasic release: By tweaking things like the type of surfactant and cholesterol level, you can make niosomes that release a drug in two phases first, a quick burst, then a slower, extended release.

5.4 Nanohydroxyapatite – remineralization of enamel

Nanohydroxyapatite, or nHAp, has really changed the game in oral health. Dentists use it to fix early enamel damage and help teeth heal. It works by filling in tiny cracks in your enamel, kind of like patching up a wall. You'll find nHAp in toothpastes, mouthwashes, and gels, where it leaves behind these tiny particles that help rebuild and strengthen your enamel. Some people even say it's just as good as fluoride, maybe better. So, it's turning into a go-to option for stopping cavities from getting worse and easing tooth sensitivity.

How nanohydroxyapatite works

nHAp particles look a lot like natural tooth enamel, so they can blend in and repair spots where minerals have been lost. They don't just sit on the surface they settle right into enamel defects, filling them up and smoothing things out. As these tiny apatite particles patch up the damaged areas, the enamel gets harder and stronger. This added strength helps protect teeth from developing cavities in the first place, since it stops more minerals from washing away. When you use nHAp with fluoride, the two work even better together, boosting the repair process. Plus, some research shows nHAp has antibacterial properties, which means it can give extra protection against dental problems.

Applications in oral care

- Toothpaste: Some toothpastes use nHAp as an active ingredient to help repair and strengthen enamel every day.
- Mouthwash: You'll also find nHAp in certain mouth rinses. These target spots in your mouth that need extra help, delivering the ingredient right where it's needed.
- Gels and varnishes: In gels and varnishes, nHAp gives a more concentrated treatment, focusing on specific problem areas.
- Dental sealants: Dentists sometimes apply nHAp before putting on a sealant. This fills tiny holes in weakened enamel, helps the sealant stick better, and improves remineralization more than the usual acid etching method.

5.5 Carbon-based nanomaterials (graphene, CNTs) – biofilm disruption, drug carriers

Carbon-based nanomaterials like graphene and carbon nanotubes are making waves in oral health. They break up biofilms and deliver drugs right where they're needed. Their big draw? A huge surface area and some pretty wild physical properties. These materials work well as antibacterial agents and drug carriers. Still, people worry about how safe they are and whether they'll be gentle with the body. That's the big hurdle right now.

Biofilm disruption

The anti-biofilm properties of graphene and CNTs are based on both physical and chemical mechanisms. [29]

Physical disruption

- Nano-knife effect: The sharp edges on graphene nanosheets and carbon nanotubes act like tiny blades. They can cut right through bacterial cell membranes, which makes the cell leak its insides and die.

- Enveloping and isolation: Graphene sheets don't just sit there they can wrap themselves completely around bacteria. Once trapped, the bacteria lose access to nutrients and can't multiply.
- Nanotextured surfaces: Studies on implant coatings with carbon-infiltrated nanotubes show something interesting. It's not the chemical makeup that stops biofilm growth it's the texture of the surface. The unique landscape keeps bacteria from spreading.

Chemical and synergistic effects

- Oxidative stress: Graphene and its derivatives, like graphene oxide (GO), trigger reactive oxygen species (ROS) that damage bacterial membranes and other parts of the cell.
- Electron transfer: Graphene pulls electrons from bacterial membranes, which messes with their structure and weakens them.
- Synergistic activity: Mix graphene with other antimicrobial agents zinc oxide or silver nanoparticles, for example, and the result is stronger, longer-lasting antibacterial and anti-biofilm effects, all while keeping cytotoxicity lower.

Drug delivery

As drug carriers, CBNs can improve the delivery and effectiveness of therapeutic agents in oral care.

Graphene and graphene oxide (GO)

- Carriers for antibiotics: GO's big surface area means it can carry a lot of antibiotics thanks to non-covalent interactions like π–π stacking. That lets it deliver drugs right where they're needed, targeting oral pathogens and releasing the medicine at a steady pace.
- Enhance Therapies: It doesn't stop there. GO boosts newer therapies, too. Take antimicrobial photodynamic therapy (aPDT) as an example. Here, GO can load up photosensitizers like indocyanine green (ICG), keeping them stable and making them more effective at killing tough bacteria like E. faecalis, which often causes root canal infections.
- Targeted gene therapy: GO also steps into gene therapy. It can deliver nucleic acids straight to the troublemakers like Streptococcus mutans knocking out their virulence genes.[30]

Carbon nanotubes (CNTs)

- Delivery for bone regeneration: CNTs do more than just sit there they help bones heal. When you functionalize them, they can carry growth factors right where you need new bone and tissue to grow, especially around dental implants. That's huge for anyone dealing with periodontitis.
- Multi-drug carriers: They're also great at multitasking. CNTs can haul different drugs at once think anti-inflammatories and antibiotics straight to an infected spot or a wound in your mouth. It's a targeted approach that really speeds up recovery.

6. Nanomedicine Applications in Oral Healthcare

Nanomedicine is changing the game in healthcare, blending nanotechnology with medicine and dentistry in ways that matter. In the world of oral health, these tiny materials open new possibilities for diagnosing problems, stopping disease before it starts, and treating dental issues more effectively. This review takes a closer look at how nanomedicine is making a difference from fighting bacteria and preventing cavities to helping with oral cancer and even rebuilding damaged teeth.[31]

6.1 Antimicrobial activity – targeting Streptococcus mutans, Porphyromonas gingivalis

Bacteria like Streptococcus mutans and Porphyromonas gingivalis are the main troublemakers behind dental caries and gum disease. Lately, nanomedicine has stepped in with some fresh ideas think nanoparticles, nanogels, and nano-emulsions to target these infections right at the source. Silver, zinc oxide, and chitosan nanoparticles don't just carry medicine; they fight bacteria themselves by breaking up cell membranes and messing with biofilms.[31] Nano-emulsions help antimicrobial agents dissolve better and reach deeper, while nanogels hang around longer in the mouth, slowly releasing drugs where they're needed.

6.2 Periodontal therapy – nanogels, nano-emulsions, nanoparticles for local drug delivery

Nanogels, nano-emulsions, and nanoparticles are cutting-edge tools for delivering drugs right where they're needed in periodontal therapy.[32] Unlike older treatments that have a hard time keeping the medication focused and long-lasting in the tricky environment of the periodontal pocket, these new platforms get the job done.

6.3 Remineralization – nanohydroxyapatite toothpastes and varnishes

Remineralization therapy helps restore minerals lost from enamel and dentin. Nanohydroxyapatite (nHAp) stands out because its structure and makeup are so close to what's found in real teeth. Toothpastes and varnishes with nHAp work by delivering calcium and phosphate ions right where they're needed. They fill in tiny cracks in the enamel and help cut down on sensitivity. The result? Smoother, harder tooth surfaces that stay healthy longer and are better protected against cavities.

6.4 Dental caries prevention and management

Nanotechnology is changing how we prevent and treat dental cavities. By adding nanoparticles to things like dental fillings, sealants, and other materials, dentists get stronger, longer-lasting results that also fight off bacteria. Silver and zinc oxide nanoparticles, along with calcium phosphate, help stop cavity-causing bacteria and even help enamel heal. Some advanced nanomaterials go a step further they sense changes in pH and release fluoride or calcium right when your teeth need it, which means more precise and effective repair.

6.5 Oral cancer diagnosis & therapy – nano diagnostics, photothermal therapy, targeted chemotherapeutics

Nanomedicine really changes the game for spotting and treating oral cancer early. With nano diagnostics, doctors get sharper images, spot biomarkers more easily, and zero in on tumors using things like nano sensors, quantum dots, and gold nanoparticles. On the treatment side, nanocarriers make chemotherapy more targeted and cut down on those nasty side effects.[33] Then there's photothermal therapy gold and carbon nanoparticles soak up light and turn it into heat, wiping out cancer cells but leaving healthy ones alone. Altogether, these tools make treatment more precise and give patients a much better shot at a good outcome.

6.6 Regenerative dentistry – nano scaffolds for pulp and bone regeneration

Regenerative dentistry is all about bringing damaged dental tissues like pulp, dentin, and bone back to life or swapping them out for new ones. Scientists use nano scaffolds made from biodegradable polymers and bioactive nanoparticles to copy the natural environment around cells.[34] This setup helps cells stick, grow, and turn into the right kind of tissue. By packing nanofibers and nanocomposites with growth factors, researchers boost the body's ability to heal and regenerate tissue. These tiny, carefully designed scaffolds play a big role in regenerating dental pulp and restoring bone in the jaw. Honestly, they're opening some exciting new possibilities in dental tissue engineering.

7. Nano-Diagnostics in Dentistry

Nano-diagnostics in dentistry is a pretty exciting field right now. It's all about using nanotechnology to spot and track diseases both in your mouth and throughout your body right down at the molecular level. These tools aren't just fast; they're incredibly sensitive and accurate, catching diseases long before you'd notice any symptoms.

One of the coolest developments? Saliva-based nano sensors. Scientists are using tiny particles think gold, carbon nanotubes, and magnetic materials, to pick out disease markers hiding in your spit.[35] Since saliva carries DNA, RNA, proteins, and enzymes that give away clues about your overall and oral health, these nano sensors can flag specific molecules linked to things like oral cancer, cavities, gum disease, and even big-picture issues like diabetes or heart disease. What's great is that these sensors are non-invasive and easy to use, and they give you results almost instantly. That makes them a real asset in dental clinics and for broader health screenings.

There's also a lot happening with nano-biosensors. These gadgets bring together biological parts like antibodies, enzymes, or nucleic acids and nanomaterials that turn those biological reactions into signals we can measure. In dentistry, they're making a real difference in catching oral cancers, especially squamous cell carcinoma, and spotting precancerous changes early by detecting tumor markers, microRNAs, or cancer-specific proteins at incredibly low levels. Plus, they can keep tabs on things like glucose in people with diabetes or inflammation markers for heart disease, all through saliva. Because they're so precise and can spot several biomarkers at once, dentists can diagnose problems on the spot and get people the care they need right away.

Imaging has gotten a big boost from nanotech, too. Quantum dots tiny, glowing semiconductor particles let dentists see molecular and cellular changes in oral tissues more clearly. They can be tweaked to latch onto cancer cells, bacterial colonies, or inflamed spots, which helps with pinpoint diagnosis. Other nanoparticles, like gold, iron oxide, and silica, ramp up the power of MRI, CT, and fluorescence imaging by making the images sharper and more detailed. Gold nanoparticles, for example, make it easier to spot oral lesions during optical imaging, while iron oxide ones improve MRI scans of both bone and soft tissue. These tools are opening the door to earlier disease detection and even pave the way for therapies that use imaging to guide treatment.[36]

8. Commercial Nanomedicine-Based Oral Healthcare Products

Nanomedicine in oral healthcare isn't just some distant idea; it's already shaking up the way dentists treat, prevent, and fix dental problems. We're way past just toothpaste and mouthwash with nanoparticles mixed in. These days, nanotechnology pops up everywhere in dentistry. Take antimicrobial coatings, for example. Dental tools, implants, and even fillings may get a layer of silver, titanium dioxide, or zinc oxide nanoparticles.[37] That stops bacteria from sticking around and forming biofilms, which means fewer infections and cleaner mouths.

Implants have gotten a serious upgrade, too. Now, they come with nanoscale coatings or surface tweaks that help them bond faster with bone and heal quicker. Titanium implants coated with hydroxyapatite or silica nanoparticles, for instance, help bone lock onto the implant and cut down on recovery time. Fillings and sealants have changed nanocomposites as well make them stronger, more durable, and better-looking than old-school materials.

If you think this all sounds futuristic, think again. There are plenty of nanotech dental products already cleared by the FDA and marked for use in Europe. Nano Care Gold and Nano Care Plus use silver nanoparticles to fight germs in oral hygiene products. Toothpastes like Colgate Sensitive Pro-Relief and Apagard have nano-hydroxyapatite particles that patch up enamel and ease sensitivity. Nano Met implants, used in the EU, rely on titanium tweaked at the nanoscale for better bone bonding. Nano Silver Gel, another FDA-cleared product, uses those same silver nanoparticles to treat mouth sores and wounds.[38] So, nanotechnology isn't just for labs anymore. It's out there, in clinics, making a real difference.

On the business side, the market for nanomedicine in oral health is taking off. People want better-looking teeth, more advanced treatments, and, honestly, there are just more oral health problems to deal with. Analysts expect the nano dentistry sector to grow about 10 to 12 percent each year over the next decade.[39] What's driving that? Innovations in nano-coatings, better regenerative materials, and smart drug delivery systems that target oral tissues. North America and Europe are leading the way, thanks to strong tech adoption and regulatory backing from agencies like the FDA and EMA. But Asia-Pacific isn't far behind. Dental tourism is booming there, and governments are investing heavily in new healthcare tech, so growth is expected to be even faster.

Bottom line? Nanomedicine is changing the game in dentistry. We're seeing safer, longer-lasting, and more effective treatments everything from antimicrobial coatings and nano-engineered implants to new diagnostic materials. With more research, solid regulations, and people becoming more aware of these options, nano dentistry is only going to grow. The future of dental care looks a lot brighter, and a lot more high-tech, than ever before.[40]

9. Safety, Toxicity, and Regulatory Concerns

Nanomaterials are making a big splash in dentistry these days. They offer real advantages, like killing harmful bacteria and making fillings or coatings stronger.[41] But you can't ignore the flip side there are real questions about safety, toxicity, and how these new materials should be regulated. Since these tiny particles interact right at the molecular level with gums and teeth, their biocompatibility is a huge deal. Silver, zinc oxide, and titanium dioxide nanoparticles get used all the time for their antimicrobial punch and added strength. But their size lets them slip into cells and even push through biological barriers.

Most research points out that, if dentists use the right amounts, these nanoparticles play nice with oral tissues. Go overboard though, or use them for too long, and you might see problems irritation, inflammation, or oxidative stress in the mouth. The way each nanoparticle behaves depends on its surface charge, shape, and how easily it dissolves. These factors really shape how they interact with the cells in your mouth and, ultimately, how safe they are. That's why researchers pay close attention to both the local effects in the mouth and what happens if these particles get into the rest of the body.

Studies in nanotoxicology show that, in some cases, nanoparticles can move past the mouth's defenses and enter the bloodstream through the gums or oral tissues. Once inside, they sometimes build up in organs like the liver, lungs, kidneys, or even the brain.[42] That's where the real worry comes in. Take silver nanoparticles, for example they fight bacteria well, but at high doses, they can spark the creation of reactive oxygen species, which can damage DNA and proteins inside cells. Titanium dioxide nanoparticles, when inhaled during manufacturing or dental work, might irritate the lungs. Still, most dental nanomaterials are designed to stay put on the teeth or gums, so they don't usually end up in the bloodstream.

Researchers keep digging into how much exposure is safe, how these materials break down, and what long-term impacts they might have.[43]

On the regulatory front, agencies like the FDA in the U.S. and the EMA in Europe have set up rules for how nanotech-based dental products get tested and approved. The FDA decides if a product counts as a drug, device, or biologic and then asks for a deep dive into the particle size, how the particles are spread out, their surface chemistry, and their safety profile. The EMA takes things case by case, focusing on how the nanomaterials interact with the body and how safe they are from start to finish. There aren't global rules everyone follows yet, but both agencies agree on one thing: every product needs solid pre-clinical testing, clinical trials, and ongoing monitoring after it hits the market.

Of course, ethics matters, too. Dentists and researchers have a responsibility to be upfront with patient's people need to know both the upside and the risks of treatments that use nanomaterials. Informed consent isn't just paperwork; it's about making sure patients really understand what's involved. Researchers and manufacturers also need to stick to ethical standards in their studies, treating both animals and people responsibly.[44]

At the end of the day, balancing innovation with patient safety is the guiding principle for nanodentistry's future.

10. Challenges and Future Perspectives

Table 3: Challenges and Future Perspectives

Challenges	Explanation	Future Perspectives	Expected Benefits
1. Toxicity and Safety Issues	Long -term effect of nanoparticles on oral tissues and body systems are not fully understood.	Development of biocompatible and non-toxic nanomaterials.	Safer nanomedicine-based oral products for daily or clinical use.
2. Limited Clinical Research	Most nanomedicine studies are in laboratory or animal models not human trials	Conducting a large scale clinical trial to confirm safety and efficacy.	Evidence-based approval and widespread clinical application.[45]
3. Regulatory and Ethical Barrier	Lack of clear global regulations nanomedicines use in dentistry	Establishment of standardized testing, ethical guidelines, and regulatory frameworks.	Faster approval, ethical usage, and patient trust.
4. High Manufacturing Cost	Production and stabilization of nanoparticles increase cost of dental product.	Green synthesis and cost-effective nano-fabrication methods.	Affordable nanomedicine therapies accessible to all.
5. Stability and Controlled Drug Release	Difficulty in maintaining nanoparticle stability and precise drug release in oral environment.	Creation of smart nano-carriers and stimuli-responsive delivery systems.	Targeted, sustained drug release improving treatment outcomes.
6. Environmental Concerns	Improper disposer of nanomaterials may contaminate water and soil.	Development of eco-friendly nanomaterials and recycling methods.	Reduced environmental pollution and sustainable nanodentistry.
7. Integration with Existing Dental Materials	Compatiblity issues between nanomaterial and convensional dental polymer and metals.	Designing hybrid materials with improved bonding and bioactivity.	Enhanced strength, antibacterial action, and tissue regeneration.

CONCLUSION

Nanomedicine represents a major advancement in oral healthcare by overcoming the limitations of conventional dental products and therapies. Nanoscale materials and delivery systems provide enhanced antimicrobial action, targeted drug delivery, improved enamel remineralization, early disease diagnosis, and effective tissue regeneration. Applications of nanoparticles, nanogels, liposomes, and nanoscaffolds have demonstrated promising outcomes in managing dental caries, periodontal disease, oral cancer, and implant integration. However, concerns related to long-term toxicity, biocompatibility, large-scale clinical validation, and regulatory standardization remain significant challenges. Future research should focus on developing safe, cost-effective, and biodegradable nanomaterials supported by robust clinical trials. With proper regulation and ethical implementation, nanomedicine has the potential to revolutionise dentistry by enabling next-generation, personalized, and preventive oral healthcare solutions.

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