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Fabrication and Functionalisation of Green Nanoparticles for Periodontal Drug Delivery

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Abstract: ***Periodontal disease is an infection of the gums and supporting tissues of the teeth.[1] Usual treatments like cleaning and giving antibiotics do not fully remove the bacteria from deep pockets.[2] Nanoparticles, because of their very small size, can carry medicines directly to the affected site and release them slowly [3]. There are different methods of making nanoparticles of which "green synthesis" using plant extracts or natural products is gaining attention as it is safe, cheap, and eco-friendly [4]. This article explains how green nanoparticles are fabricated and can be functionalised for periodontal drug delivery and their possible use in treating periodontal disease [5].***

Keywords: periodontal disease, green synthesis, nanoparticles, drug delivery, eco-friendly treatment

1. Introduction

Periodontal disease is an infection of the gums and supporting tissues of the teeth [6]. It ranges from gingivitis, a reversible gum inflammation, to periodontitis, which leads to bone loss and tooth loss if untreated [7]. Globally, periodontitis affects nearly 10–15% of adults severely, making it a major oral health problem [8]. The disease is primarily caused by bacterial biofilms in the periodontal pockets, which trigger an exaggerated host immune response [9]. This imbalance between microbial challenge and host defense results in tissue destruction and disease progression [10].

Conventional treatments such as scaling and root planing help in removal of plaque and bacteria from the teeth and gums but they often cannot reach deep into the pockets around the teeth [11]. Oral medicines like antibiotics are sometimes given but they may not reach the infected area in the right concentration and may cause side effects in other parts of the body [12].

Nanotechnology, a recent advancement, offers a new way to treat periodontal disease [13]. Nanoparticles are extremely tiny particles, much smaller than a cell, which can carry drugs directly to the infected site. Because of their small size, nanoparticles can penetrate bacterial biofilms that protect harmful bacteria and stay in the gum pockets for a longer time. This allows the drugs to be released slowly and work more effectively [14].

Among different types of nanoparticles, green nanoparticles are the ones gaining attention recently. These are made using natural sources such as plant extracts, herbs, or microbes instead of harmful chemicals. This makes them safer, cost-effective, and environmentally friendly. Green nanoparticles can be further modified to carry antibiotics or other therapeutic agents and can also help in reducing inflammation and promoting tissue healing. Overall, nanoparticles provide a targeted, efficient, and safe method for delivering drugs in periodontal therapy, offering a modern approach to improve treatment outcomes for gum diseases [15].

The main objective of this review is to discuss the role of nanoparticles in the management of periodontal disease and how they can improve drug delivery compared to conventional methods. The scope of this review includes an overview of periodontal disease, the need for advanced drug delivery systems, different types of nanoparticles used in periodontics, their advantages, and their potential future applications [15].

Role of Nanoparticles in Periodontal Drug Delivery

Nanoparticles are extremely small carriers of drugs, usually measuring between 1 to 100 nanometers in size. Because of their unique size and surface properties, they behave differently compared to conventional drug delivery systems. In periodontics, they are gaining importance to treat gum diseases, especially in cases where routine cleaning or antibiotics alone are not enough.

Nanoparticles have the ability to reach areas in the periodontal pocket that are difficult to access with traditional treatments. The deep gum pockets harbor bacteria in biofilms, which are resistant to antibiotics. Due to their tiny size, nanoparticles can easily penetrate into these deep pockets and deliver drugs right at the site of infection.

It has the capacity for controlled and sustained drug release. Unlike conventional gels or mouthrinses where the medicine quickly washes away with saliva, nanoparticles can hold the drug and release it slowly over time. This ensures that the medicine stays active for a longer duration, reducing the need for frequent applications.

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Nanoparticles also improve drug stability and bioavailability. Some drugs degrade quickly or do not dissolve well in the mouth. When these drugs are loaded into nanoparticles, they become more stable and are protected from early breakdown, which allows them to act more effectively against harmful bacteria. Nanoparticles also help to minimize side effects. In systemic antibiotic therapy, the medicine spreads throughout the body, which may lead to unwanted reactions and bacterial resistance. With nanoparticles, the drug is targeted only to the diseased gum tissues, so the healthy parts of the body are not exposed to unnecessary medication [16,17].

Green synthesis of Nanoparticles

Green synthesis of nanoparticles is an eco-friendly and sustainable approach that uses biological systems such as plants, bacteria, fungi, and algae for nanoparticle production. Unlike conventional chemical and physical methods that may involve toxic chemicals, high energy, or hazardous byproducts, green synthesis relies on natural reducing and stabilizing agents found in biological extracts. Plant-based synthesis, for example, makes use of phytochemicals like flavonoids, alkaloids, phenols, and proteins to reduce metal ions into stable nanoparticles [18].

Principles of green Nanotechnology

The principles of green nanotechnology in the synthesis of nanoparticles focus on sustainability, safety, and efficiency. They include the use of renewable natural resources such as plants and microorganisms, replacing toxic chemicals with non-toxic reducing and stabilizing agents. Water and other safer solvents are preferred over hazardous ones, and the processes are designed to occur under mild conditions, reducing energy consumption. Waste prevention and minimization of harmful byproducts are emphasized, along with the use of biodegradable and biocompatible materials to ensure safety for both humans and the environment. These principles ensure that nanoparticle production is eco-friendly and aligns with sustainable practices [19].

The importance of sustainability and biocompatibility

Sustainability and biocompatibility are two key aspects of green synthesis of nanoparticles. Sustainability ensures that the synthesis process uses renewable resources, eco-friendly solvents, and low-energy methods, thereby reducing environmental pollution and conserving natural resources. This makes the process long-term viable and less harmful to ecosystems. Biocompatibility is crucial because nanoparticles are often intended for biomedical, pharmaceutical, or environmental applications where direct interaction with living systems occurs. Biocompatible nanoparticles minimize toxicity, reduce side effects, and improve safety for human use [20].

Biological source for green synthesis

Biological sources play a vital role in the green synthesis of nanoparticles, as they provide natural reducing and stabilizing agents. The major biological sources include plants, bacteria, fungi, algae, viruses, actinomycetes, biomolecules. Leaves, stems, roots, fruits, seeds, and flowers that are rich in phytochemicals like flavonoids, alkaloids, terpenoids, phenolics, and proteins act as reducing and capping agents. Certain bacterial species can reduce metal ions and produce nanoparticles intracellularly or extracellularly. Filamentous fungi and yeasts secrete enzymes and metabolites that help in nanoparticle formation. Both microalgae and macroalgae contain biomolecules like polysaccharides, proteins and pigments useful in nanoparticle synthesis. Some viruses can also act as nanostructure templates due to their unique protein coats. These microorganisms produce secondary metabolites that facilitate nanoparticle synthesis. Biomolecules such as proteins, amino acids, enzymes, sugars, and polysaccharides can serve as reducing and stabilizing agents.

Among these, plants are the most widely used source because they are safe, easily available, cost-effective, and rich in diverse biomolecules [21,22].

Nanoparticles used in periodontal therapy

In periodontal therapy, several types of nanoparticles are being explored because of their antimicrobial, regenerative, and drug-delivery potential. The main types include:

1) **Metal and Metal Oxide Nanoparticles**
- Silver nanoparticles (AgNPs)
- Zinc oxide nanoparticles (ZnO NPs)
- Gold nanoparticles (AuNPs)
- Titanium dioxide nanoparticles (TiO_2 NPs)

2) **Polymeric Nanoparticles**
- Chitosan
- PLGA (poly lactic-co-glycolic acid)
- Alginate

3) **Lipid-based Nanoparticles**
- Solid lipid nanoparticles (SLNs)
- Nano structured lipid carriers (NLCs)

4) **Ceramic Nanoparticles**
- Calcium phosphate or hydroxyapatite nanoparticles

5) **Carbon-based Nanoparticles**
- Carbon nanotubes
- Graphene oxide

6) **Silica Nanoparticles**
- Mesoporous silica nanoparticles (MSNs)[23].

Fabrication of Green Nanoparticles

The first step is to prepare the plant extract, which provides the natural chemicals to make nanoparticles. Fresh and healthy plant parts like leaves, stems, or fruits are picked and washed well with clean water to remove dirt. Then the plant material is dried and ground into fine powder. The powder is then boiled in water or ethanol to release the plant compounds and is filtered to remove solid plant bits, leaving only the extract.

The second step is, synthesis of the nanoparticles where the plant extract is mixed with a solution of metal salts to form nanoparticles. A metal salt like silver nitrate ($AgNO_3$) or gold chloride ($HAuCl_4$) is dissolved in water. The plant extract is slowly added to the salt solution while stirring and sometimes heating. As the reaction happens, the solution changes color, showing nanoparticles are being formed (for example, silver nanoparticles look brownish). The solution is kept for a certain time and temperature for completing the process.

The third step is purification and isolation where the solution is spun at high speed to collect the nanoparticles as a pellet at the bottom. This step is called centrifugation.

Then the pellet is washed with clean water to remove any leftover plant compounds or unreacted salts and dried to get a fine powder

Then characterization is done where the nanoparticles are checked whether it is formed properly using techniques like UV-Vis spectroscopy which confirms nanoparticle formation by detecting special light absorption peaks; Microscopy that helps to see the size, shape, and structure of the nanoparticles; Zeta potential and particle size analyser that measures the charge and average size, which tell us about the stability; FTIR that shows which plant compounds helped in reducing and capping the nanoparticles.
The last step in processing is to check if the nanoparticles can be used to treat gum diseases. For that three tests are carried out; antimicrobial test, antioxidant test and the cytotoxicity test [18,24,25].

Optimizing Green Nanoparticles for targeted drug delivery
After nanoparticles are made, they can be modified to improve how they work. This process is called functionalisation. Functionalisation helps nanoparticles stay stable in saliva, reach the site of infection better, and release drugs for a longer time.
In this first, Coating with polymers is done where natural materials like chitosan or alginate can be used to cover nanoparticles. This makes them safer and allows slow release of drugs. Then Loading with antibiotics like doxycycline, metronidazole, or chlorhexidine can be attached to the nanoparticles. After that special proteins or peptides can be added so that nanoparticles directly attack the periodontal bacteria. Some nanoparticles can be designed to release the drug only in certain conditions, like the acidic environment inside gum pockets. This is called as Smart release systems [26,27]

Functional role in periodontal therapy
1) **Antimicrobial Action:** Green nanoparticles especially silver, zinc oxide, and gold nanoparticles exhibit strong antibacterial activity against *Porphyromonas gingivalis*, *Aggregatibacter actinomycetemcomitans*, and other periodontal pathogens that helps in reducing bacterial load within periodontal pockets [28].
2) **Anti-inflammatory Effect:** They help to decrease the inflammatory response by regulating cytokine levels and reducing oxidative stress [29]
3) **Drug Delivery:** Green nanoparticles can be used as carriers for antibiotics, anti-inflammatory drugs, or growth factors. Their small size and high surface area enable controlled and sustained drug release at the infection site [28,29]
4) **Tissue Regeneration:** Certain nanoparticles such as hydroxyapatite or calcium phosphate nanoparticles promote bone and connective tissue regeneration, aiding in the repair of damaged periodontal structures [30]
5) **Biofilm Disruption:** Green nanoparticles can penetrate and disrupt bacterial biofilms [28]
6) **Biocompatibility and Safety:** Green nanoparticles are less toxic and more compatible with human cells, supporting safe and sustainable periodontal therapies [29,30]

Available Nanoparticle-Based Drug Delivery Systems [31,32,33]

1) Nanoparticles
- Deliver drugs in a controlled and sustained manner.
- *Example:* Chitosan nanoparticles loaded with chlorhexidine.

2) Nanoliposomes
- Carry both water- and fat-soluble drugs effectively.
- *Example:* Liposomal doxycycline for periodontal pockets.

3) Nanospheres / Nano-capsules
- Provide controlled and targeted drug release.
- *Example:* PLGA nano-capsules containing metronidazole.

4) Nanogels / Hydrogels
- Offer prolonged local drug release and good tissue adhesion.
- *Example:* Green-synthesized hydrogel loaded with antibiotics.

5) Nanofibers
- Used for localized drug delivery and tissue regeneration.
- *Example:* Electrospun nanofiber mats releasing growth factors.

6) Dendrimers
- Can carry multiple drugs for controlled release.
- *Example:* PAMAM dendrimers carrying anti-inflammatory drugs.

7) Solid Lipid Nanoparticles (SLNs)
- Protect drugs from degradation and allow slow release.
- *Example:* SLNs containing curcumin or triclosan.

8) Nano-emulsions
- Improve solubility and enhance drug penetration.
- *Example:* Nano-emulsion gel containing clindamycin.

9) Magnetic Nanoparticles
- Enable targeted drug delivery using magnetic fields.
- *Example:* Iron oxide nanoparticles guided to periodontal sites

2. Limitations

Even though green nanoparticles look promising, there are still some problems they are,
1) Plant extracts are not always the same, so results can vary.
2) Long-term effects in the mouth are not fully known.
3) Making them in large amounts is not easy.
4) More studies are needed before approval for use in patients [34,35]

3. Future Approaches

In the future, green nanoparticles could make periodontal treatment more targeted and effective by delivering drugs directly to infected areas. They might be used with stem cells or growth factors to help regrow lost bone and tissue. Smart nanoparticles that release drugs only when needed could reduce side effects, and combining antimicrobials and anti-inflammatory drugs in one system could improve healing. Also, eco-friendly production and using nanoparticles with diagnostic tools could make treatments safer, more sustainable, and tailored to each patient [36,37].

4. Conclusion

Green nanoparticles are a promising and eco-friendly way to treat gum diseases like periodontitis. They are made using natural plant extracts, which makes the process safe, cheap, and less harmful to the environment. These nanoparticles are very small, so they can reach deep into gum pockets where normal treatments cannot. They can kill harmful bacteria, break down biofilms, carry medicines for longer release, and even support the healing of gums and bone. Scientists have also shown that nanoparticles can be changed on their surface to make them more stable and effective. This makes them a useful option for local drug delivery in dentistry. However, even though the early results are very positive, most studies are still in the lab or animal models. More clinical trials and safety studies are needed before these nanoparticles can become a regular part of dental treatment [38,39].

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