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Review Article

Chitosan nanoparticles and its role in endodontics

Naveen Thangarasu

Post Graduate Student, Department of Conservative and Endodontics, SRM Dental College, Chennai -600020 Tamil Nadu, India.

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ABSTRACT

Natural materials like chitosan are frequently present in the environment. One of the many cationic polysaccharides found in nature is chitosan. It is a naturally occurring biopolymer created from chitin, a material found in crustacean shells. Chitosan has remarkable chemical and biological qualities that have piqued endodontic researchers' attention in dental science. Natural alternatives for use in endodontic procedures are constantly being researched and evaluated because to the potential negative effects of regularly used synthetic medications and other safety-related factors. Based on selected publications that were published in recent years, the study discusses the potential use of chitosan in endodontic treatment. The purpose of this review is to evaluate the use of chitosan particles in endodontics and dental care.

***Keywords:** Chitosan particles, nanoparticles, antimicrobial, endodontics, bacterial cell, nanodentistry*.

Address for Correspondence:
Naveen Thangarasu,
Post Graduate Student, Department of Conservative and Endodontics, SRM Dental College, Chennai -600020 Tamil Nadu, India.
Phone No: +91 9486869634
Email: naveenthangarasu@gmail.com

INTRODUCTION

Unbonded particles can be found in nanoparticles, which can be accidental, natural, or man-made materials. Nanoparticles are special because they have a significant surface area, are small, and have higher chemical reactivity. The substantial differences between nanomaterials' properties are a result of the ratio of surface to volume being enhanced and the amount of atoms at the surface. being more numerous as compared to micro-/macrostructures.[1] Nanoparticles come in a variety of sizes and shapes. According to their dimensions, they can be divided into four groups: nanoparticles with a size of zero, nanorods with a dimension of one, thin films with a dimension of two, and nanocones with a dimension of three.[2] Numerous biological applications, including tissue regeneration, medication delivery systems, antimicrobial use, gene modification, and imaging systems, have been made possible by nanotechnology as a science and technology. Utilizing nanomaterials, biotechnology, including tissue engineering, and nanorobotics, nanodentistry will enable the support of perfect oral health.[3,4,5] Trends in oral health and illness may shift the emphasis away from diagnoses and treatments. The few nanoparticles utilized in dentistry are the subject of this review. The application of nanomaterials in endodontics is concentrated on techniques that would enhance dentin matrix, mechanical uprightness, and antibacterial healing of previously sick tissue. A novel technology is currently being investigated in endodontics to overcome microbial problems.[6]

The different nanostructures include[2]-

1. Nanopores
2. Nanotubes
3. Quantum dots
4. Nanoshells
5. Dendrimers

Nanocomposites:

Discrete nanoparticles are uniformly dispersed and nonagglomerated in resins or coatings to produce nanocomposites. An alumino - silicate material with a refractive index of 1.508 and an overall average molecule dimension of 80 ran, as well as a 1:4 M proportion of alumina to silica, were both components of the utilized nanofiller.[7]

Advantages:

1. Excellent toughness
2. Better flexural strength, elasticity modulus, and translucency
3. Reduced filling shrinkage by 50 %
4. Outstanding handling capabilities

Local anesthesia

In nanodentistry, the gingiva of the patient will be injected with a colloidal fluid comprising millions of active, analgesic micron-sized dental robots. Before reaching the surface of the tooth's crown or the oral mucosa, the nanoparticles must first transit via the gingival sulcus, lamina propria, and dentinal tubules in order to reach the pulp. After the analgesic dental robots have been implanted in the pulp, the dentist can command them to turn off all sensitivity in any particular tooth that requires treatment. When the oral technique is finished, the dentist positions the nanorobots to reinstate all sensation, release control of nerve movement, and exit the tooth via the same paths utilized for entry.

Impression Materials

A unique siloxane additive for impression materials is made by mixing vinylpolysiloxanes and nanofillers. The substance has increased hydrophilic properties, improved flow, and better detail clarity.

Nanosolutions

The unique and dispersible nanoparticles that are delivered by nanosolutions can be used as bonding agents. The adhesive will always be perfectly mixed thanks to the homogeneity this ensures.

Silver Particles

Dental resin composites have been thought to contain silver ions as antimicrobial elements. After 24 or 72 hours of incubation, the modified tissue conditioner combined with silver nanoparticles shown antibacterial effects against S. aureus, S. mutans, and C. albicans fused.[8]

Nanocapsulation

The South West Research Institute has developed innovative antibodies, anti-microbials, and drug delivery methods in discharge frameworks that enclose nanocapsules with reduced reactions. Osaka University in Japan created a display that shows how to deliver characteristics and medications specifically to the human liver in 2003. Empty nanoparticles containing a peptide essential for the infection's propagation through the liver in humans were formed by designated Hepatitis B contaminated envelope L particles. Future tailored nanoparticles may be designed to specifically target oral tissues, including periodontium-derived cells.

Nanoneedles

Nano crystal-infused suture needles have been created. Nanoneedles are also known as Sandvik Bioline, RK 91TM needles. Nanotweezers are additionally being worked on which will make cell-surgery conceivable sooner rather than later.

Nanoirrigants

Nanoparticles clean the root canal system while preventing bacterial adhesion. Ca $(OH)^2$ particle sizes ranged from 1 to 2.5 m on average.[9] Nanoparticles are much smaller, ranging in size from 40 to 250 nm. The surface area is multiplied by ten when there is such big variation. Consequently, the active exchange surface increased in comparison to Ca $(OH)^2$.

Other Nanoparticles

1. Filtration masks, protective garments, and antipathogenic nano emulsions and nanoparticle
2. Devices for quick healing in medicine
3. Delivery platform for hemostatic agents: biodegradable nanofibers
4. Both nanocrystalline silver particles with antimicrobial properties and nanofibers made of silk are being developed for use as wound dressings.
5. A biomaterial made of calcium phosphate has been developed. This bone biomaterial flows and interdigitates with existing bone effectively like a pliable adhesive. It promotes the development of bone and cartilage cells.

Antibacterial mechanisms of nanoparticles

Nanoparticles have recently drawn a lot of interest in the medical community because they have superior antibacterial properties compared to those of conventional antimicrobial drugs and a low risk of developing bacterial resistance. The antibacterial activity of nanoparticles against various microbes varies depending on the type of nanoparticle and from that of the original bulk state.

The simultaneous action of two separate mechanisms is thought to be the reason why the nanoparticles are effective at destroying bacterial cells. One includes the electrostatically induced attachment of nanoparticles to the membrane of the target bacterial cell, altering the membrane potential, depolarizing the membrane, and ultimately inducing membrane integrity loss. Major bacterial cell activities like respiration, the movement of nutrients, and energy transduction are disrupted as a result. This finally results in the death of bacterial cells. In the second stage, oxygen free radicals are produced, including reactive oxygen species (ROS), which could also impair protein function, erase DNA, and produce an excessive quantity of radicals, all of which can harm the viability of the bacterial cell.[10]

Nanoparticles' antimicrobial effectiveness in endodontics

In vitro research have lately investigated many types of nanoparticles in various formats to determine how effective they are against endodontic infections. According to their nature, the nanoparticles used in these investigations can be roughly divided into three categories: polymeric, non-organic, metallic or inorganic, and bioactive nanoparticles.

Chitosan Nanoparticles

Polymeric nanoparticles laden with antimicrobials have also been researched for endodontic antimicrobial delivery. Nanoparticles are stabilized by biopolymers which prolong their release time, thus improving antimicrobial properties of polymeric nanoparticles. The polymers considered in nanotechnology include polyvinyl pyrrolidone, polyethylene glycol, alginate, and chitosan.

Researchers have become quite interested in polymeric nanoparticles because of their biocompatibility and antibacterial qualities. One of the most often studied polymeric nanoparticles in endodontics is chitosan (Cs-NPs). The second most prevalent natural biopolymer is chitosan (poly [1, 4-b-D-glucopyranosamine], a DE acetylated derivative of chitin). Depending on the physical properties or intended use of the nanoparticles, chitosan could be produced utilizing a variety of techniques. Biomedicine makes extensive use of chitosan. Yeast, fungus, and certain microbes also contain chitosan. 2deoxy-2-(acetylamino) glucose serves as the chitin polymer's main structural component. By creating (1,4) glycosidic connections, these units joined together to create a long chain linear polymer. Chitin is insoluble in the majority of solvents, but chitosan is soluble in the majority of organic acidic solutions with a pH lower than 6.5, including formic, acetic, tartaric, and citric acid. They are insoluble in both phosphoric and sulfuric acid. There are several different sub-atomic weights and deacetylation levels of chitosan available. Atomic weight and degree of acetylation. The primary variables influencing particle size, formation, and aggregation are atomic weight and deacetylation level.[11]

Despite numerous studies evaluating chitosan's antimicrobial potency, its antibacterial mechanism is still unknown. The substance's cationic composition has led to the development of several ideas. Chitosan that has a low molecular weight may enter bacterial cell membranes, bind to DNA, and prevent transcription and mRNA synthesis. The elements of the bacterial cell wall that are negatively charged were assumed to attach to high molecular weight chitosan, creating an impenetrable barrier that impeded transit inside the cell. Another theory for how chitosan exerts its antibacterial properties is that it can adhere to negatively charged bacterial cell membranes, making them more permeable and ultimately causing the release of cytoplasmic contents and

bacterial cell death. Others claimed that by reducing enzyme activity, chitosan's ability to chelate metals hindered the growth of bacteria. It has been proven that the presence of certain tissue components inside the root canal system, including dentine powder, dentine matrix, and pulp tissue remnants, inhibits the antibacterial properties of several endodontic disinfectants.

CS-NPs were primarily created for use in gene, medication, and antimicrobial delivery. Chitosan is highly effective against bacteria, viruses, and fungi. Gram positive bacteria are more vulnerable to infection than Gram negative bacteria. Depending on the organism, pH, degree of deacetylation (DD), molecular weight, chemical changes, and presence of lipids and proteins, the lowest inhibitory doses fall between 18 to 5000 ppm. The extent of deacetylation is known to influence the antibacterial effect. In contrast to chitosan, which demonstrated greater antibacterial activity, there are more amine groups per glucosamine unit with higher degrees of deacetylation. This improves the antibacterial action of chitosan particles. As a result, Chitosan nanoparticles are a viable drug delivery system. [12]

The antibacterial effectiveness of chitosan nanoparticles against the E. faecalis biofilm on cow root dentin was evaluated after they were treated with phosphorylated chitosan, chitosan conjugated with rose bengal, and a combination of the two. Depending on the different treatment methods employed, E. faecalis biofilm formation was inhibited to differing degrees. The addition of CS-NP and zinc oxide nanoparticles to a resin and zinc oxide-based root canal sealant improved its antibacterial function and ability to disperse the antibacterial component. The root canal sealer's flow properties were unaffected by the inclusion of nanoparticles.[13]

According to Kishen et al., the root canal treated with cationic antibacterial nanoparticles and chitosan significantly reduced the attachment of E. faecalis to dentin.[1] Such surface treatment would theoretically prevent the development of bacterial biofilms and recolonization. Later, it was determined whether CS-NPs and zinc oxide could clean up and remove E. faecalis biofilms. These nanoparticles had a concentration- and time-dependent effect on the removal of biofilms, and they continued to have an antibacterial effect after 90 days. To improve root canal disinfection utilizing ultrasonics, CS-NPs can be supplied inside the dentinal tubules and anatomical complexity of an infected root canal. Colony-forming units in infected collagen membranes and agar culture plates were considerably reduced when CS-NPs and chlorhexidine were combined.

Because of the neutralizing effects of various tissue inhibitors, utilizing antibacterial medicines inside the root canal space can be difficult. The antibacterial impact of CS-NPs was strongly decreased by tissue inhibitors such pulp and serum albumin, whereas dentin, the dentin matrix, and lipopolysaccharides had no effect on the effectiveness of CS-NPs. Major drawbacks for CSNPs included the impact of tissue inhibitors and the longer treatment period necessary to achieve efficient bacterial eradication. This called for strategies to address these flaws in upcoming research on the use of CS-NPs.[14]

Biocompatible glass

BAG attracted a great deal of interest largely because of its osteo-inductive and antibacterial effects in numerous orthopaedic and dental applications. Three distinct methods have been used to investigate the antibacterial activity of BAGs. BAG is made up of CaO2, SiO4, Na2O, and P2O5 in varying amounts, and its antibacterial activities rely on the local physiological changes.

Numerous antibacterial properties of bioactive glass are important for endodontic applications. Improved root canal sanitation has been investigated using BAGs in micro and nano forms. By being able to release its ions when it encountered an aqueous medium, raise the pH in the immediate area, increase the osmotic pressure surrounding the bacterial cell, which inhibited bacterial growth, and precipitate calcium and phosphate ions in

the bacterial cell membrane, the bioactive glass material's antimicrobial property was demonstrated. which interfered with the bacterial cell's normal functions. Amorphous nanometric BAG that was between 20 and 60 nm in size was used by Zehnder et al.[15] Studies on in vitro root canal cleaning revealed that BAG had a considerably lower antibacterial impact than calcium hydroxide did in limiting the formation of lingering germs. The micrometric counterpart of the nanometric BAG has a significantly higher alkaline capacity and greatly improved biofilm removal due to its increased specific surface area. Compared to biofilm bacteria, they did a superior job of eliminating planktonic bacteria.[16] Due to the micro-10 BAG's fold higher silica release and solution pH elevation of more than 3 units, the nano-antibacterial BAG's efficacy is significantly lower than that of the latter. 45S5 bioactive glass nanoparticles were discovered to exhibit higher antibacterial activity against E. faecalis in comparison to micro sized bioactive glass particles. The release of sodium and calcium ions as well as the incorporation of protons into the glass cause the root canal systems to have a high pH, which is unfavourable to microorganisms. As a result, the osmotic pressure will rise (beyond 1%), which many bacteria find inhibiting.[17]

Silver nanoparticles

The publications most frequently discussed the antibacterial characteristics of silver nanoparticles. The negatively charged bacterial cell membrane is blocked from functioning by silver nanoparticles until the bacterium eventually explodes. The cytoplasmic substance will subsequently be penetrated by the nanoparticles, which will then interact with the DNA and RNA's sulfate- and phosphorus-containing proteins, severely harming the bacterial cell. When in contact with an aqueous solution, the silver nanoparticles also emits silver ions, which further lowers bacterial activity.[18]

Wu et al. assessed the effectiveness of silver nanoparticles against the biofilm produced by Enterococcus faecalis in two different forms: as two distinct concentrations of a gel (0.02% and 0.1%) and as an endodontic irrigant solution at a concentration of 0.1%. The E. faecalis biofilm was not significantly altered by the treatment. The E. faecalis biofilm was more likely to be damaged by using gel-based silver nanoparticles with a 0.02% concentration. than it was by 0.01%, which increased the number of live bacteria. It has also been demonstrated that incorporating silver nanoparticles improves the antibacterial effects of calcium hydroxide and other intra-canal medications.

Ag-NPs with bacterial-killing properties may be employed to clean up root canals. It needs a long contact period to kill bacteria effectively, therefore its usage should ideally be restricted to medicine beside as an irrigant.

Most of the nanoparticles studied for disinfecting root canals rely on contact-mediated antibacterial activity that is time-dependent. By preventing the growth of both on the surface and at the resin-dentin contact have biofilm, the addition of different nanoparticles to root filling material sealers greatly increased the antibacterial efficacy.

When used as an antibacterial agent against endodontic infections, silver nanoparticles were extremely effective. To assess any impact on the tooth structure's colour stability, more study is required about damaging effects of the dentine surface on human cells.[19]

Magnesium-containing nanoparticles (Mg-NPs)

Due to their well-known antibacterial capabilities, magnesium-containing nanoparticles have been proposed for use as antibacterial agents against gram-positive and gram-negative bacteria, spores, and viruses. Both magnesium-halogen nanoparticles, which comprise chlorine, bromine, and fluorine, and magnesium-oxide nanoparticles can include magnesium. The penetration's facilitation of the nanoparticles' effects on DNA binding and lipid peroxidation led to additional destruction of the bacterial cell. The presence of magnesium-

oxide nanoparticles in an aqueous state was demonstrated to be bactericidal due to the effect of superoxide anions formed on the bacterial cell surface.[20]

Regarding endodontic pathogens such E. faecalis, S. aureus, and Candida albicans, Monzavi et al. investigated the effectiveness of various sodium hypochlorite concentrations, 2% chlorhexidine, and 5 mg/L and 10 mg/L magnesium oxide nanoparticles as antibacterial agents. According to the findings, there were no discernible differences between the tested endodontic pathogens and the irrigant solutions' antibacterial efficacies. Compared to sodium hypochlorite, the addition of magnesium oxide nanoparticles to an irrigant prolonged the antibacterial action.[21]

Nanoparticles of zinc oxide (ZnO-NPs)

High antibacterial activity was demonstrated by zinc oxide nanoparticles, which destroyed microbial cells in an environment with a higher pH level. To enhance the antibacterial properties of endodontic sealers and prevent bacterial recolonization in root canals, Zheng et al. demonstrated the potential advantages of utilizing ZnO-NP.[22] Similar to other types of nanoparticles, zinc oxide nanoparticles' antibacterial mechanism results in Cell death, a release of cytoplasmic material, and an increase in the permeability of the cell wall membrane.

It has been demonstrated that zinc oxide nanoparticle size affects both their capacity to kill bacteria and their capacity to produce When reactive oxygen species and water interacted, they produce hydrogen peroxide. More antibacterial activity is present in organisms that are smaller in size.[23] Zinc oxide nanoparticles inside the bacterial cell release zinc ions, which interfere with the enzymatic system and the metabolism of amino acids, further harming the bacterium. It has been demonstrated that the antibacterial efficacy of zinc oxide nanoparticles varies with concentration, with greater concentrations having the highest antibacterial impact. According to research, zinc oxide nanoparticles' antibacterial potency is proportional to their concentration, with larger concentrations having the greatest antibacterial effect. The addition of zinc oxide nanoparticles to a resin-based root canal sealant demonstrated the antibacterial effect. In addition, 95% less E. faecalis was able to establish a biofilm on the dentinal walls. Different levels of antibacterial activity were shown against P. aeruginosa, E. faecalis, C. albicans, S. aureus, and Kocuria rhizophila when zinc oxide nanoparticles and polyethylene glycol were mixed to make a foamy combination and used as an intra-canal medication.[24]

Calcium-deficient hydroxyapatite nanoparticles loaded with tetracycline

To develop an osteoconductive drug delivery system that can facilitate the administration of tetracycline medication into the periodontium, Madhumathi and Kumar employed apatite nanocarriers in 2014. They created varied Ca/P ratios of calcium-deficient hydroxyapatite (CDHA) nanoparticles. The proliferation of human periodontal ligament fibroblast cells and their antibacterial activity were shown to have enhanced. The calcium-insufficient hydroxyapatite nanoparticles can be considered osteoconductive bone replacements with proliferative and antimicrobial capabilities for various periodontal applications.[24]

Triclosan loaded Poly Lactic-co-Glycolic acid nanoparticles

Antimicrobial agent triclosan is non-cationic in nature. It is well known for being effective against certain bacteria that cause plaque. Because of their huge surface area, NPs quickly release TCS, and Pinon-Segundo et al. hypothesized that TCS-NPs would help reduce gingival inflammation during periodontal therapy.[25]

Bioactive mesoporous calcium silicate nanoparticles

Wu and associates developed injectable bioactive mesoporous calcium silicate nanoparticles with high specific surface area and pore volume for potential application in filling an apical region of the root canal. It has been shown to support periodontal ligament cells' osteogenic development and cause apatite mineralization without cytotoxicity. It also displayed sustained ampicillin administration and antibacterial effectiveness.[26]

Photodynamic Therapy Using Nanoparticles

Several studies have been conducted recently on the idea of photodynamic treatment (PDT) employing antibacterial drugs based on nanoparticles. Free radicals are created by PDT by activating them with low-energy light (such as singlet oxygen). Bacterial cell walls, membrane proteins, and nucleic acids are the principal targets of the highly reactive singlet oxygen. PDT's antibacterial action, however, was shown to be somewhat restricted. This was due to the interaction between photosensitizers and tissue inhibitors, which in turn caused a decrease in the singlet oxygen's half-life after photoactivation and a decrease in both binding to and uptake into bacterial cells.[27,28]

CONCLUSION

Although it sounds like science fiction, we dentists will instruct patients to rinse with a solution containing millions of small machines called "nanoassemblers" in order to treat even the tiniest sign of an oral disease. These tiny workers will swarm to the patient's mouth and eradicate the disease and bacteria causing the condition after receiving signals from a dentist-controlled computer.

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