



# INTERNATIONAL JOURNAL OF ADVANCE RESEARCH, IDEAS AND INNOVATIONS IN TECHNOLOGY

ISSN: 2454-132X

Impact Factor: 6.078

(Volume 10, Issue 5 - V10I5-1149)

Available online at: <https://www.ijariit.com>

## Nanomaterials in Endodontics: Applications and Scope

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### Abstract

*Advancements in nanotechnology have led to numerous potential applications in dentistry, with nanomaterials becoming increasingly significant in endodontics.<sup>1</sup> Nanosized particles, like clusters of small numbers of atoms or molecules in nanostructured biomaterials, have shown significantly superior properties in biomedical research compared to the same materials at larger scales of measurement.<sup>2</sup> These unique mechanical and chemical properties help nanomaterials to have various applications in endodontics such as obturating materials, sealers, antimicrobials, retro-filling materials, root repair and regeneration. The improved antimicrobial property of the nanomaterials is helpful in eradicating bacterial load in the canals which can be incorporated in the form of irrigants and medicaments. Applications in regenerative endodontics are currently underway creating improved scaffolds and growth-factor delivery.<sup>2</sup> This review throws insights on the current knowledge and scientific applications of nanomaterials in the field of endodontics as well as its potential future scope.*

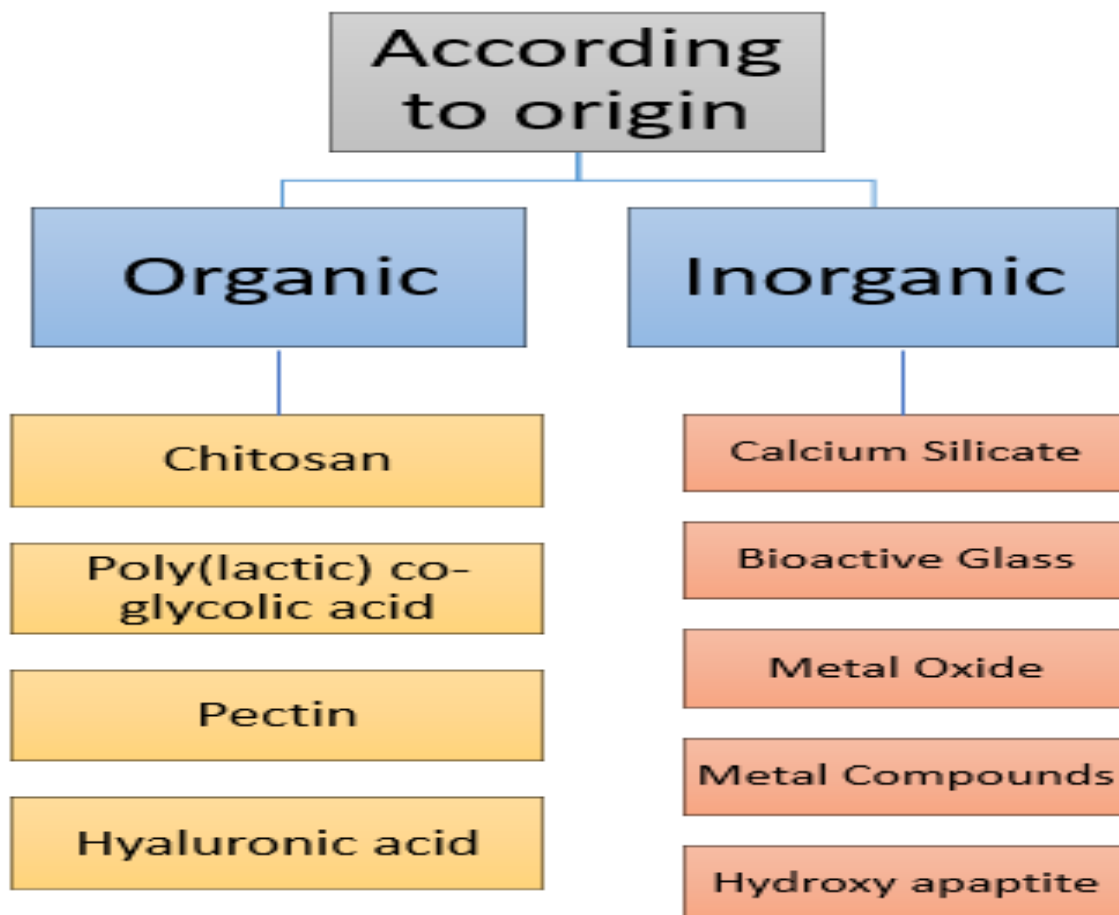
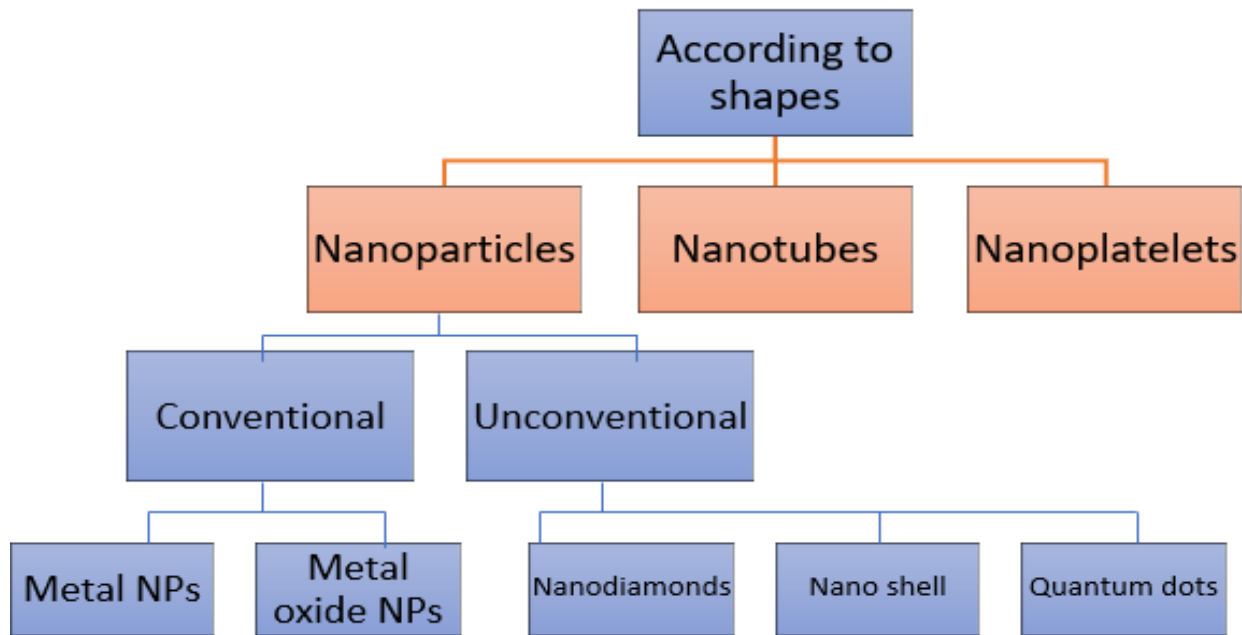
**Key Words:** Nanomaterials, Endodontics, Nanotechnology, Silver Nanoparticles, Chitosan.

### Introduction

Nanotechnology employs mechanisms to control the size and morphology of particles within the desired nano range to achieve specific objectives. When applied to the field of dentistry, this extension of nanotechnology is known as 'Nanodentistry' a term invented by Freitas.<sup>3,5</sup> Nanomaterials are substances that have been reduced to a size range of 1 to approximately 100 nanometers (1 to ~ 100 x 10<sup>-9</sup> meters). The definition by European Commission states that 'nanomaterials encompass solid particles of natural, incidental, or manufactured origin and at least 50% of their number-based size distribution falls within the range of 1 to 100 nm'.<sup>6</sup>

At this scale, the properties of materials can change dramatically. Characteristics such as solubility, reactivity, spectroscopic behaviour, electrical and magnetic properties, and membrane transport differ significantly from those of the same materials at larger particle sizes.<sup>4</sup> This phenomenon, known as the "size effect," arises from the nanoscale dimensions of nanomaterials. Various properties like elevated surface energy, different spatial confinement, decrease in structural imperfections, and larger proportion of surface atoms are improved. Different types of nanomaterials used include organic, inorganic, and oxides, ceramics, polymers, glass, silver compounds and many more.

## Classification of Nanomaterials



Endodontics is the branch of dentistry that deals with the dental pulp and the area surrounding the dental pulp. It is needed that the agents to travel to the innermost part of the canal to carry out their function effectively. With their significantly higher specific surface areas, nanomaterials are ideally suited for a wide range of applications like biocatalysis, molecular interactions in drug delivery systems, and energy-related uses.<sup>5</sup>

Research into the application of nanotechnology in various treatment areas of endodontics are underway for most efficient outcomes. It has been suggested that the enhanced wear and fatigue resistance of nanomaterials can be utilized for surface modifications of the rotary nickel-titanium files currently used in root canal therapy.<sup>7</sup>

Current studies show the improved antimicrobial properties of silver nanoparticles and calcium-silicate nanoparticles, adding as an alternative to traditional antibacterials, leading to elimination of issues of antibacterial resistance.<sup>8</sup> In case of teeth whitening, nanoparticles not only function as abrasives but also release reactive oxygen species and help remineralization.<sup>9</sup> Nanotechnologies also allow the construction of biomimetic scaffolds. Scaffolds of natural nanofibers are known to support endodontic regeneration.<sup>10</sup> The incorporation of nanomaterials in various endodontic areas like medicaments, irrigants, sealers, obturating materials, whitening agents, restorative materials and tissue regeneration are discussed.

## Applications in Endodontics



## Discussion

**1.Irrigants-** The success of endodontic treatment depends on the eradication of microbes from the root-canal system and prevention of reinfection. The root canal is shaped with hand and rotary instruments under constant irrigation to remove the inflamed and necrotic tissue, microbes/biofilms, and other debris from the root-canal space.<sup>11</sup> Sodium hypochlorite is regarded as the gold standard for chemical disinfection of root canals in endodontic treatment.<sup>12</sup> However, it can cause toxic damage to tissue. Hence, the various nanoparticles which can be used as irrigants include-

- Silver Nanoparticles-A low concentration of silver nanoparticles have demonstrated superior biocompatibility compared to sodium hypochlorite. Moreover, silver nanoparticle-based irrigation solutions have proven to be as effective as sodium hypochlorite in eliminating both *Enterococcus faecalis* and *Staphylococcus aureus*.<sup>13</sup> According to a study, silver nanoparticle was capable of binding to the infected canal surfaces despite a single, short-term (5 min) treatment.<sup>14</sup> Consequently, some researchers have proposed using silver nanoparticle solutions for root canal irrigation during endodontic treatment.<sup>13</sup>
- Chitosan NPs- chitosan a cationic biopolymer has been of a great interest in the recent past mainly due to its low toxicity and bio-adhesive properties. It's positive charge allows the complex formation with oppositely charged molecules, interacting readily with negatively charged compounds. Such complexes may be used as delivery systems for incorporating a number of bioactive compounds to reduce biofilm bacteria.<sup>15</sup>

**2.Intracanal Medicaments-** Intracanal medicaments serve as anti-inflammatory and antibacterial agents that can be utilized between appointments. They come in the form of pastes, gels, or points, which are inserted into the canal. Calcium hydroxide [Ca(OH)<sub>2</sub>] is the most frequently used medication in endodontics, primarily because of its alkalinity. The hydroxyl ions it releases lead to cell membrane distortion, protein denaturation, and DNA damage. Several nanoparticles have been utilized to eliminate the negative properties of calcium hydroxide and increase its effectiveness.

- Chitosan NPs- The biological usage of Chitosan-NPs either alone or in combination with other compounds have inhibitory effects against both Gram negative and Gram positive bacteria. This bioactivity is predisposed by numerous factors including chemical nature of Chitosan, concentration, pH, and size of the particles.<sup>17</sup> Incorporating CNPs into pastes of Ca(OH)<sub>2</sub> could potentially be beneficial when using interappointment intracanal medications because of their ability to kill bacteria in short- and long-term exposure.<sup>18</sup>
- Metal/Metal oxide NP's- **Silver nanoparticles** (20 nm in size) can be combined with calcium hydroxide, resulting in enhanced antibacterial activity compared to using calcium hydroxide alone or in conjunction with chlorhexidine. A commercially available product NanocarePlus Silver and Gold (NanoCare Dental, Nanotechnology, Katowice, Poland) has shown promising antimicrobial properties as an intracanal medicament.<sup>19</sup>

CuNPs can penetrate the bacterial cell wall, resulting in cellular damage. In the cell, nanoparticles indirectly alter DNA or protein synthesis, inactivate their enzymes, and promote the generation of hydrogen peroxide. In a study the antibacterial activity of CuNPs on a biofilm of *E. faecalis* and *S. mutans* was checked. It was possible to detect an immediate action and an over-time effect, gradually reaching their highest efficacy on day 7 after application with comparison to calcium hydroxide.<sup>20</sup>

**Zinc oxide nanoparticles (ZnO NPs)** exhibit antimicrobial effects against a broad spectrum of microorganisms by generating reactive oxygen species (ROS) and penetrating the outer cell membrane or entering the cytoplasm. ZnO NPs can inhibit the growth of *Candida albicans*, as well as *Porphyromonas gingivalis*, *Prevotella intermedia*, *Fusobacterium nucleatum*, *Aggregatibacter actinomycetemcomitans*, and *Enterococcus faecalis*.<sup>21</sup>

- Calcium Silicate NP's- Calcium-silicate NPs such as  $\text{Ca}(\text{OH})_2$  NPs, bioactive glass, and mesoporous silica NPs are also used for endodontic medicaments. Compared with conventional micrometer-sized particles,  $\text{Ca}(\text{OH})_2$  NPs (<100 nm) are considered to penetrate deeper into dentinal tubules, and this gives improved antimicrobial actions against *E. faecalis* at depths up to 400  $\mu\text{m}$  within dentinal tubules.<sup>1</sup>

**3. Obturating materials-** The ideal properties of a root filling material remain as suggested by Grossman in 1978 include easy handling and ample working time, seal the canal laterally and apically conforming to the complex internal anatomy, dimensionally stable, non-irritant, does not stain the tooth structure, antimicrobial, impervious and non-porous, unaffected by tissue fluid, radiopaque and easily removable.<sup>22</sup> Gutta-percha is the most widely used material for the root canal filling. Research indicates that gutta-percha, even when thermoplasticized, does not achieve sufficient three-dimensional filling on its own and should be used in conjunction with sealers.<sup>23</sup>

- Nanodiamonds- Lee et al developed a nanodiamond–gutta-percha composite (NDGP) embedded with nanodiamond–amoxicillin (ND-AMC) conjugates, aimed at reducing the likelihood of root canal reinfection and improving treatment outcomes. Nanodiamonds (NDs), which are carbon nanoparticles about 4–6 nm in diameter, are readily processed from waste byproducts for biomedical applications. This study demonstrated that functionalizing conventional gutta-percha (GP) cones with amoxicillin-loaded nanodiamonds (NDs) can enhance the success rate of endodontic therapies by eradicating pre-existing microbes and preventing root canal reinfection. Additionally, the incorporation of NDs increased the mechanical robustness of GP, thereby improving its handling properties during clinical use.<sup>24</sup>
- Silver Nanoparticles- Dianat and Ataie have introduced nanosilver gutta-percha to enhance the antibacterial properties of conventional gutta-percha by coating it with nano silver particles.<sup>27</sup> This provides a significant antibacterial effect against *Candida albicans* and several bacteria, including *Enterococcus faecalis*, *Staphylococcus aureus*, and *Escherichia coli*.<sup>25</sup> There is no difference in cytotoxicity towards fibroblasts or in the subcutaneous tissue reaction and inflammation between gutta-percha coated with silver nanoparticles and conventional gutta-percha.<sup>26</sup>

**4. Sealers** Even with extensive research to improve gutta-percha's properties, a sealer is still required for effective three-dimensional filling of the canal system. Researchers have investigated silver (Ag), calcium oxide (CaO), copper oxide (CuO), zinc oxide (ZnO), chitosan (CS), magnesium oxide (MgO), and QAPEI nanoparticles as potential antimicrobial agents and for enhancing physicochemical and biological properties.<sup>23</sup>

- Silver Nanoparticles- Silver nanoparticles exhibit significant antimicrobial activity and, notably, possess the capability to circumvent typical mechanisms of resistance formation.<sup>28</sup> This effectiveness has been observed across multiple sealers, including AH Plus, Endosequence, MTA Fillapex, Sealapex, and Tubliseal. A silicone-based sealer (polydimethylsiloxane) has been enhanced with nanosilver, termed NanoSeal-S.<sup>1</sup>
- Bioceramic nanomaterials- A bioceramic-based nanomaterial, known as EndoSequence BC sealer, has been developed for clinical use. It comprises calcium phosphate, calcium silicate, calcium hydroxide, zirconia, and a thickening agent. The nano additives enable efficient material delivery through 0.012 capillary needles and conform to irregular dentin surfaces. This material sets and hardens rapidly, resulting in a strong seal and dimensional stability. Upon setting, hydroxyapatite formation occurs, imparting bioactivity and compatibility. Moreover, the high pH of 12.8 provides antibacterial properties.<sup>30</sup>

#### Organic nanomaterials

- Chitosan- The incorporation of chitosan nanoparticles (NPs) extended the antibacterial effectiveness of commercial endodontic sealers, even after one month, by decreasing the total and viable biovolume of *E. faecalis*. Recent findings underscore the capacity of chitosan nanoparticle-containing nanocomplexes, such as carboxymethyl chitosan/ACP nanocomplexes (<40 nm), to accomplish intrafibrillar mineralization of collagen, facilitating dentine repair. By utilising this biomimetic approach, chitosan/hydroxyapatite nanocomposites blends with tricalcium silicate sealer enhanced the physico-mechanical properties of endodontic sealers and strengthens root dentin fracture resistance.<sup>31</sup>
- Quaternary ammonium compound (QAC) NPs- Quaternary ammonium compound (QAC) nanoparticles, such as quaternary ammonium polyethylenimine (QPEI) NPs, demonstrate strong antibacterial properties. QPEI nanoparticles have been incorporated into existing sealers such as AH Plus, GuttaFlow, and Epiphany. These nanoparticles extend the antibacterial activity of the sealers without compromising their mechanical properties. Additionally, QPEI nanoparticles exhibit high stability, do not release by-products into the environment, and maintain biocompatibility while retaining strong antibacterial activity.<sup>1,30</sup>
- Nanomaterials as nanocarriers for sealers- Nanocarriers like halloysite nanotubes (HNTs) and multiwalled carbon nanotubes (MWCNTs) show significant promise for use in endodontic sealers. HNTs, in particular, with their distinctive tubular structure, can effectively encapsulate antimicrobial agents, thereby boosting the antibacterial effectiveness of methacrylate resin-based root canal sealers.<sup>32</sup>

**5. Root Canal Repair/Root end filling-** To seal the root canal effectively, the properties of root end filling material play a very important role. With MTA being the mainstream material for root end filling, some of its disadvantages exist which have been tried to overcome by the use of nanomaterials.

- Silver nanoparticles- According to a study, the experimental calcium silicate-based cement with the incorporation of silver nanoparticles and calcium chloride had favourable physicochemical properties that can be useful to maintain a bacteria-free environment and for improved healing, which are necessary in root-end surgeries.<sup>33</sup> The addition of silver nanoparticles (Ag NPs) enhances calcium ion release from mineral trioxide aggregate (MTA), which is essential for promoting new bone tissue growth and accelerating the healing process. Incorporating silver nanoparticles (Ag NPs) is reported to reduce the setting time of mineral trioxide aggregate (MTA), accelerate the hydration of silicates, and potentially enhance the material's utility.
- Other nanomaterials that are incorporated into MTA to enhance its properties are- bismuth lipophilic NPs, Silver-zeolite NPs and TiO<sub>2</sub> NPs.

**6. Regeneration** - Maintaining pulp vitality is essential for the functional life of a tooth. To achieve this, active and living biomaterials are necessary to avoid the current drastic treatment method, which involves removing all cellular and molecular content regardless of its regenerative potential. Nanomaterials for dental pulp regeneration can be utilized on their own or in combination with growth factors, drugs, or stem cells.<sup>11</sup> Nanofibrous based scaffold- Nanofibrous and microporous membranes hold significant promise for promoting dental pulp regeneration by mimicking the extracellular matrix. Functionalizing nanofibers with nanoreservoirs of BMP-2 or BMP-7 has proven highly effective for bone regeneration and enhances the differentiation of mesenchymal stem cells (MSCs), thereby accelerating tissue regeneration in vivo.<sup>10,34</sup> Various nanofibrous microporous scaffolds create an optimal environment for dentin regeneration.

1. **Tooth Whitening agents-** Hydrogen peroxide and carbamide peroxide are commonly used whitening agents in clinical dental care and aesthetics. However, the free radicals produced by these agents can cause pathological damage, leading to ongoing concerns about their safety. Recent advancements in the development of nanoparticles and their applications in various tooth whitening fields are explored.<sup>9</sup>
2. **Restorative Materials-** Last but not the least, one of the greatest discoveries in the field of nanodentistry includes the incorporation of nanoparticles in restorative materials like composite resin and glass ionomer cement.

**Nanocomposites-** Nanofillers incorporated in composites have elevated properties like translucency, good handling skills, better surface finish and contouring.<sup>29</sup> This has stem from the current ongoing research for eliminating or reducing the polymerization shrinkage, improving aesthetics and wear resistance of composites.<sup>37</sup>

**Nano Glass Ionomers-** The incorporation of nanomers and nanoclusters in fluoroaluminosilicate (FAS) glass has led to significant advancements in resin-modified glass ionomers. Since their clinical introduction in 2007, these nanotechnology applications have enhanced the aesthetics and polishability of final restorations.<sup>29</sup>

## Conclusion and Prospects

The expanding research on nanomaterials in endodontics highlights their potential in addressing root canal infections and facilitating tissue repair. Nanoparticles offer promising enhancements in antibacterial, anti-adhesive, and drug delivery applications for endodontic treatments. However, it is important to note that most current evidence stems from preliminary studies, necessitating further investigation through animal and in vivo research. This ongoing research is crucial for unlocking the full potential of nanomaterials in advancing endodontics and enhancing patient outcomes. Some future prospects of this evergrowing technology includes the use of 3D printing, nanozymes and nanobots.

Chau et al. developed a vancomycin-releasing polycaprolactone/nHA nanocomposite using 3D modeling. Inorganic nanoparticles exhibiting enzyme-like properties are referred to as nanozymes. They are characterized by being less expensive, easy to synthesize, more stable, and highly efficient compared to their natural counterparts.<sup>3</sup> Dasgupta et al. introduced the use of magnetic nanobots in root canal procedures. These nanobots have the capability to penetrate deeper into the dentin, a feat challenging with conventional methods. Additionally, the unique retrieval process of nanobots presents an improved option.

These nanobots operate using specialized algorithms or software.<sup>3,35</sup> While NPs have shown considerable potential in endodontic applications, several issues remain to be addressed, including biocompatibility, human safety, ethical considerations, and economic factors. The application of nanoparticles (NPs) necessitates careful consideration due to potential cellular repercussions, including the induction of apoptosis, inhibition of cell growth, genotoxicity, and neurological and respiratory damage. Nanodentistry is an emerging field with significant potential, offering new techniques for the diagnosis and treatment of dental diseases. Consequently, the future of dentistry and endodontics is poised for further progress and transformation through advancements in nanotechnology.

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