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RESEARCH ARTICLE

NANO-ANTIMICROBIALS IN ENDODONTICS

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Abstract

A root canal system exhibits a challenging environmental condition about the availability of nutrients and oxygen. Usually, chemical antimicrobials (topical) are used within the root canals in combination with mechanical instrumentation to achieve "microbe-free" root canals before obturating the root canal with an inert filling material. Antimicrobial resistance (AMR) has emerged as one of the primary public health problems of the 21st century. It threatens the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, viruses, parasites, and fungi which is no longer susceptible to the currently used antibiotics. One of the important requirements of endodontic treatment is the ability to eliminate microorganisms from the root canal system and prevent re-entry of microbes. This antimicrobial effect is achieved by a combination of chemical and mechanical disinfection. Due to increasing antimicrobial resistance, the efficacy of traditionally used irrigants has been decreased. Owing to the limitation of currently used antibiotics it paves way for nano antimicrobial-based irrigants.It has been emphasized that the addition of antibacterial nanoparticles in root canal sealers would upsurge the direct (based on the direct antibacterial assay) and diffusible antibacterial effects (based on a membrane-restricted antibacterial assay) of the root canal sealers. Additionally, nanoparticles when incorporated into intracanal medicament have shown added benefits.Nanoparticle-based photosensitizers have been considered to potentiate the antimicrobial efficacy of photodynamic therapy (PDT). The antibacterial nanoparticle-based treatment has the potential to improve antibacterial/ antibiofilm efficacy. They have distinct advantages when applied in endodontics. The whole concept of nanotechnology in health care should be accepted with positive zeal for future development. This review paper describes the scope of nano antimicrobials in endodontics as irrigants, intracanal medicaments, and their role in photodynamic therapy, sealers, and obturating materials.

Introduction:-

Nanotechnology is a well-known field of research since the last century. Since' 'Nanotechnology "was presented by Nobel laureate Richard P. Feynman during his famous 1959 lecture "There's Plenty of Room at the Bottom"(Feynman, 1960), there have been various revolutionary developments in the field of nanotechnology (1).

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Progress in the medical implementations of nanotechnology has resulted in the formation of a new field called nanomedicine (2). This concept was first put forward in 1993 by Robert A. Freitas Jr. and was defined as "Observing, controlling, and treating the biological systems of the human body at the molecular level using nano-structures and nano-devices"(3).

R.A. Freitas Jr., in the year 2000, coined the term "nano dentistry" which implies the application of nanomaterials and dental nanorobots towards diagnosis and treatment, intending to improve comprehensive oral health.

Nanomaterials are materials whose component size ranges from 0 to 100 nm in at least one dimension. The word "nano," which is derived from the Greek word (nannos) meaning "dwarf," is a prefix that refers to 1 billionth of physical size (4).

A nanomaterial is defined as "an insoluble or biopersistant and intentionally manufactured material with one or more external dimensions, or an internal structure, on the scale from 1 nm to 100 nm" (5).

Nanomaterials are classified based on their dimensions, the materials used, and the origin of the materials (6).

Based on the composition, nanoparticles are generally classified as either naturally occurring or synthetic (Table 1)(7). They are further categorized as organic or inorganic in nature. Based on the shape, they are classified as particles, spheres, tubes, rods, plates, and so on. Functionalized nanoparticles are those that have a core of 1 material and additional molecules or proteins bonded on its surface or encapsulated within. Depending on the specific applications, nanoparticles can be functionalized with peptides, drugs, photosensitizers, and so on (8). The core nanoparticles can be used as a convenient surface for molecular assembly and may be composed of inorganic or organic materials. An additional layer of linker molecules is required to proceed with functionalization wherein the linker molecules have reactive groups at both ends that bind various moieties like antibodies, fluorophores, and so on onto the core nanoparticle.

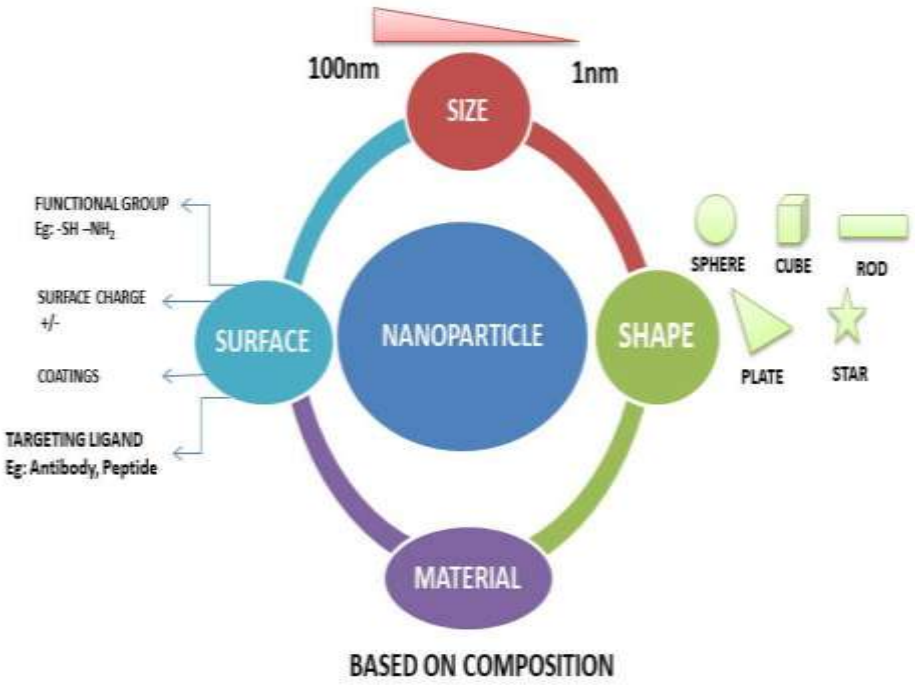


Table 1:- Nanoparticles available based on the composition.

Inorganic	Metallic	Polymeric	Quantum dots	Functionalized with
Zinc oxide	Gold	Alginate	Cadmium sulfide	Drugs
Iron oxide	Silver	Chitosan	Cadmium selenide	Photosensitizers
Titanium dioxide	Iron			Antibodies

Cerium oxide	Copper			Proteins
Aluminum oxide	Magnesium			
Bioactive glass				

Shrestha A, Kishen A. Antibacterial Nanoparticles in Endodontics: A Review. J Endod. 2016 Oct; 42(10):1417-26.

Nanomaterials have distinct advantages in that they display unique physicochemical properties when compared to their bulkier counterparts due to their nanoscale sizes and high surface-area-to-volume ratio (9).

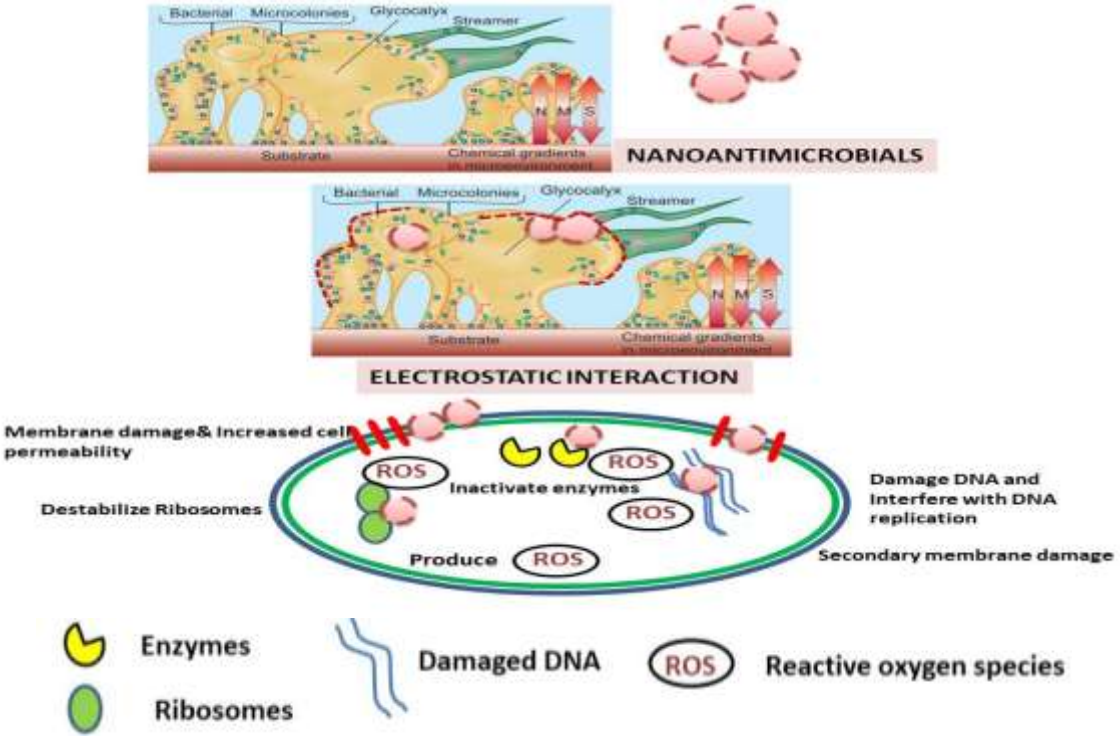
This includes increased reactivity, greater solubility, biomimetic features, and the ability to be functionalized with other materials such as drugs, bioactive molecules, and photosynthesizers (9) (10). Furthermore, antimicrobial nanoparticles can easily permeate biofilms, are effective at smaller doses and may help alleviate the increasing use of antibiotics (11).

These advantages are being exploited for progressive research in the field of endodontics to design highly specific materials and devices to interact with microbes, at the subcellular and molecular level to achieve maximal therapeutic efficacy with minimal side effects (12) to face one of the major tasks of elimination of bacterial biofilms surviving within the anatomic complexities and uninstrumented portions of the root canal system during root canal treatment.

Mechanism Of Action of Nano- Antimicrobials

Biofilms containing bacteria are protected by a self-produced matrix of extra-polymeric substance (EPS). This suppresses the infiltration of root canal disinfectants and reduces their efficacy (13). Furthermore, anatomically complex regions in the root canal system may be inadequately debrided, resulting in residual infection. In addition, irrigants are often unable to reach the depths of dentinal tubules, allowing the persistence of bacteria (14). Furthermore, the use of antibiotics is highly debatable. Due to the shortcomings of the conventional root canal disinfection techniques, newer nano antimicrobials have are being tested for their efficacy.

Given the physicochemical properties of nano antimicrobials, they can permeate into biofilms and interact electrostatically with bacterial cell walls, which leads to cell membrane injury, increased cell permeability, generation of reactive oxygen species, interference with cellular functions, destruction of proteins, DNA damage and ultimately, cell death (Figure 1) (11),(15),(16)



Endodontic Irrigation

Effective chemical and mechanical debridement are essential to eliminate root canal infection. However, biofilm bacteria benefit from a variety of factors that help improve their survival.

Conventional Irrigants	Properties	Drawbacks
Sodium hypochlorite (NaOCl) 0.5% to 5.25%.	Tissue dissolving and antimicrobial properties (1)	Breakdown and weakening of the organic dentin matrix(2) Damage to the periapical tissues(2)
Chlorhexidine 2%	Antibacterial property& Substantivity(3)	Inability to degrade necrotic tissue (3) Reduced efficacy against Gram-negative microbes(3)
Ethylenediaminetetraacetic acid (EDTA) 17%	Chelating agent(4)	Excessive use can lead to dentin demineralization and erosion (4)

Considering the limitations of the aforementioned irrigants, there is a constant and increasing body of research going on in the field of nanoparticle-based irrigants.

Silver Nanoparticles (AgNPs)

AgNPs have been widely investigated in dentistry. AgNPs exhibit antimicrobial and antifungal properties as they possess a multimode of action. The synergistic and multimode antibacterial actions markedly decrease the need for high doses of antibiotics, therefore minimizing the potential of antibiotic resistance and toxicity to the tissues (21).

AgNPs were shown to possess antibiofilm and antimicrobial efficacy against E. faecalis (22).

When used as an irrigating solution, poly (vinyl alcohol) (PVA) coated AgNPs were effective against Pseudomonas aeruginosa, Candida albicans, and E. faecalis (23).

A study reported that AgNP's antimicrobial activity was on par with conventional endodontic irrigants such as 2% chlorhexidine, 1% NaOCl, and 5% NaOCl(24).

On the other hand, some studies have probed the efficacy of AgNPs-based irrigants in comparison to conventional endodontic irrigants. AgNPs solutions were less effective in reducing viable E. faecalis in biofilm than 2% chlorhexidine after 5 minutes of irrigation and only equally effective after 15 minutes (25). Compared to both chlorhexidine and AgNPs solutions, NaOCl exhibited superior biofilm dissolving and antibacterial properties (25).

Drawbacks

Prospective staining of dentinal walls and induce discolouration (26).

The cytotoxic effects are possibly due to the production of reactive oxygen species that initiate pro-inflammatory host responses, the magnitude of which depends on the concentration, dimensions, and aggregation of AgNPs(27).

Wu et al reported that syringe irrigation of AgNPs was less effective than gel application in eliminating biofilms and also suggested the use of AgNPs as an intracanal medicament due to their contact and time-dependent nature, (22).

Chitosan Nanoparticles

Chitosan is a natural, organic biopolymer derived from chitin. Chitosan is a cationic compound that interacts with negatively charged bacterial cell membranes, which increases its permeability and leads to leakage of the intra-cellular constituents and ultimately cell death exhibiting broad-spectrum antimicrobial action (28). It is also biocompatible and has chelating abilities, making it an attractive alternative to modern root canal irrigants(29).

Chitosan nanoparticle solutions exhibit antibacterial properties against E. faecalis and antibiofilm properties (30). Chitosan nanoparticles were able to retain their antimicrobial properties after ageing for 90 days (31). However, another study found its antibacterial efficacy may depend on the state of the bacteria as planktonic bacteria were eliminated while their biofilm counterparts persisted after 72 hours (31).

Several studies have revealed chitosan's ability to act as a chelating agent and improve the wettability of dentin (30),(32),(33). Concurrently, chitosan nanoparticles showed resistance to bacterial collagenase degradation by potentially stabilizing dentin collagen (34).

Drawbacks
It has been advocated that conventional chelating agents remain are better in promoting sealer penetration, as a final rinse of Qmix® or 17% EDTA resulted in double the sealer penetration depth into dentinal tubules at 5 mm from the apex compared to a final rinse of chitosan nanoparticles (35).

The prolonged treatment time and contact-dependent nature of chitosan nanoparticle-based irrigants necessitate further research.

Other Metal and Metal Oxide Nanoparticles
Metal oxide nanoparticles are also been examined as potential endodontic irrigants.

Zinc oxide nanoparticles (ZnONPs) exhibit their bactericidal properties, with a mechanism of action similar to that of AgNPs(11). A ZnONPs-based irrigant was found to eliminate planktonic E. faecalis and disrupt the biofilm matrix, maintaining its antibacterial activity after 90 days of aging (31). However, its antibacterial efficacy was less distinct against biofilm bacteria compared to their planktonic counterparts (31).

Titanium dioxide, Magnesium oxide, and Iron oxide exhibit antimicrobial properties,(11),(36)although the research on these compounds as potential endodontic irrigants is comparably fewer.

Nano-magnesium oxide solution had long-term antimicrobial efficacy in both in vitro and ex vivo environments against E. faecalis(36).

Titanium dioxide nanoparticle solution when used as a final rinse was found to result in double the mean fracture resistance of endodontically treated teeth compared to NaOCl as the final irrigant (37).

Iron oxide nanoparticles showed peroxidase-like activity when synthesized with hydrogen peroxide, resulting in antibiofilm and bactericidal activity against E. faecalis(38).

Drawbacks
Holds a degree of cytotoxicity, hence biocompatibility studies are a must before proceeding to in vivo research (11).

Lastly, gold nanoparticles have been reported to be substantial in biomedical applications (39). However, they have not been commonly investigated for their use in endodontics, due to uncertainties regarding their antimicrobial efficacy (11).

Intracanal Medicaments
Intracanal medications are anti-inflammatory and antibacterial agents that can be used in between appointments. They are available as pastes, gels, or points that are inserted into the canal. (40)Intracanal medicament is generally recommended when treatment cannot be completed in one appointment; there are chances that surviving intracanal bacteria often proliferate between appointments. (41)Calcium hydroxide is considered, one of the prototypes of the intracanal medicament used today. However, with advancements in endodontics, newer materials have emerged (42) (43).

The ability of E. faecalis to penetrate dentinal tubules and resist bactericidal action has been postulated as one of the reasons for the involvement of E. fecalis in persistent root canal infections. (44) This has led to extensive research in endodontics for an alternative intracanal medicament. CHX gluconate (2%) has been recommended as a potential alternative to calcium hydroxide (43). Other medications, such as Ledermix paste, have been recommended for routine intracanal administration. Ledermix paste has been recommended as an initial dressing, especially if the patient has persistent symptoms.

Silver nanoparticles (AgNPs) are used in many disinfectants that are used in medical devices. AgNPs gets attached to the cell wall of bacteria penetrate the cell and cause increased permeability of bacterial cell membrane followed by disintegration (46)

The most used material is calcium hydroxide paste, which causes the release of hydroxyl ions, which raises the pH within the root canal, causing damage to microorganism DNA, cytoplasmic membranes, and enzymes. Silver nanoparticles (size 20 nm) can be mixed with calcium hydroxide, which has been shown to have increased antibacterial activity when used alone or in combination with chlorhexidine 8. NanocarePlus Silver and Gold (NanoCare Dental, Nanotechnology, Katowice, Poland) has demonstrated potential antimicrobial properties as an intracanal medicament. (40)

Calcium hydroxide nanoparticles have superior antimicrobial activity against E. faecalis compared to conventional calcium hydroxide in culture media as well as in dentinal tubules (47). The use of the Nano TAPC (triple antibiotic paste+Catafast-TAPC) as intracanal medicament showed the highest bacterial reduction count when compared to TAP and

$Ca(OH)_2$(41).

According to a study done by F Afkhami et al, AgNPs appear to have a good potential to be used as an appropriate Ca(OH)2 vehicle, to eliminate biofilm of E. faecal bacteria from human dentin within one week. (48)However, after a month, the effect of this carrier was insignificant from that of the CHX carrier and Ca(OH)2 per se. As a result, this vehicle is recommended as short-term intracanal medication. Before its clinical application can be considered, the potential adverse effects of AgNPs, such as cytotoxicity and the potential effect on tooth discoloration should be investigated (48).

The findings of the study done by Garrocho-Rangel et.al, suggest that Calcium hydroxide/iodoform nanoparticles may be appropriate as an alternative intracanal medicament for infected or devitalized primary teeth. Also, Calcium hydroxide/iodoform nanoparticle paste had deeper penetration through the root dentin tubules. (49)

Further studies have shown that Calcium hydroxide nanoforms and chitosan nanoforms could be more effective intracanal medicaments. Nanoparticles penetrated dentinal tubules to greater depths and demonstrated significantly greater antimicrobial efficacy against E. faecalis(47).

In a similar study conducted, groups with calcium hydroxide and either micro- or nanoparticulate zinc oxide had the largest zones of inhibition in the agar diffusion test, When the antimicrobial activity of. C. albicans, E. faecalis, and S. aureus were evaluated, they had the largest zones of inhibition in the group with calcium hydroxide-zinc oxide combination, but there was no statistical difference when compared to zinc oxide pastes(5).

Photodynamic Therapy

Photodynamic therapy combines non-toxic Photosensitisers with safe light of appropriate wavelengths to create antimicrobial properties by creating reactive oxygen species (ROS), which finally causes cell death. Despite this, PSs have several limitations, including limited water solubility, an unpredictable drug release profile, poor target selectivity, and a low extinction coefficient, which have hampered clinical usage(50). Furthermore, photo-bleaching may have unforeseen consequences and harm healthy tissues. To overcome these constraints, new precise nanomaterial devices were designed to operate as vehicles for PSs that were loaded or embedded in them or to act as PSs themselves. (50)

The sensitivity of gram-positive and gram-negative bacteria to antimicrobial photodynamic therapy differs significantly. Gram-positive bacteria are more vulnerable than gram-negative bacteria in general. As a result, different types of bacteria's structural properties must be examined. The physiology of gram-positive organisms explains their high sensitivity. The photosensitizer can pass through the cytoplasmic membrane because it is surrounded by a rather permeable layer of peptidoglycan and lipoteichoic acid (51). When microorganisms are organized in the form of biofilm or isolated cells, there are differences in susceptibility to PDT, and the challenge of PDT is greater when the microorganisms are structured in the form of biofilm (52)

In experimentally infected root canals of extracted teeth, photodynamic effects resulted in a 99 percent reduction in colony-forming units. For clinical therapy of periapical lesions in teeth undergoing single sitting endodontic treatment or retreatment, the PDT was recommended as a promising effective adjunct to routine antibacterial intracanal cleaning and shaping(53) (54) (55) (56). In addition, photodynamic effects in infected root canals of extracted teeth resulted in a 99 percent reduction in colony-forming units (57) (58)

One of the advantages of light-activated killing is that, unlike the resistance to more conventional chemical antimicrobial treatments, resistance to singlet oxygen is unlikely to spread. (59) Certain metallic nanomaterials, such as TiO2, ZnO, and fullerenes, as well as their derivatives, have proven to be capable of producing singlet oxygen and eliminating bacteria. (60) Tricyclic dyes (e.g., methylene blue, erythrosine), tetrapyrroles (e.g., porphyrins), and furocoumarins have been the most often investigated sensitizers on bacteria (e.g. psoralen).

Nanoparticles are becoming increasingly popular. The effectiveness of a mixture of biodegradable and biocompatible poly(lactic-co-glycolic acid) (PLGA) and colloidal gold nanoparticles loaded with methylene blue and exposed to red light at 665 nm against planktonic E. faecalis and experimentally infected root canals(61) The findings suggest that PLGA nanoparticles encapsulated with photoactive medicines could be a promising antibacterial endodontic therapy adjuvant. (61)

Gold nanoparticle conjugates should theoretically have improved binding and cell wall piercing characteristics, allowing for a higher concentration of photoactive molecules to be delivered (62)

Kishen et.al have mentioned, ways for combining nanoparticles with PSs , such as (I) photosensitizers supplemented with nanoparticles (ii) photosensitizers contained within nanoparticles, (iii) Photosensitizers bound or loaded to nanoparticles, and (iv) nanoparticles acting as photosensitizers themselves. (60)

Antimicrobial PDT has proven to be improved when nanoparticles and photosensitizers are combined; numerous mechanisms could be responsible for this improved antimicrobial efficacy (60)

Root Canal Sealers And Obturation Materials

Following adequate cleaning and shaping, it is important to seal the root canal system to prevent the ingress of bacteria and reduce the risk of recontamination (63). Therefore, an ideal endodontic obturation material should not only possess adequate physicochemical properties but should also exhibit some antimicrobial properties against potential surviving bacteria in the root canal(63). To overcome the various limitations, of existing Obturation Materials and Root Canal Sealer researchers are focusing on nanoparticles.

Quaternary Ammonium Compounds

Through electrostatic interaction with bacterial cell membranes, quaternary ammonium polyethyleneimine (QPEI) has shown broad-spectrum antibacterial and antibiofilm capabilities (64). Intracellular signals induced by QPEI nanoparticles also lead to programmed cell death (11). Furthermore, due to their insoluble structure, these compounds can provide long-term antibacterial effects.

QPEI nanoparticles were observed to influence osteoblast and osteoclast growth and differentiation when added to AH PlusTM, an epoxy resin-based sealer, and Pulp Canal SealerTM, a zinc oxide eugenol-based sealer (65).

Furthermore, investigations have demonstrated that commercially available sealers and QPEI nanoparticles can be used without compromising sealer cytotoxicity or physicochemical qualities such as solubility, flow, compressive strength, or dimensional stability(66) (65).

However, it has been found that adding QPEI nanoparticles to AH PlusTM did not result in a substantial increase in antibacterial efficacy. (66) Another study found that the antibiofilm effects of QPEI nanoparticle-modified AH PlusTM against E. faecalis may be strain-dependent (67).

Adding QPEI nanoparticles to Pulp Canal SealerTM, on the other hand, increased antibacterial and antibiofilm efficacy against E. faecalis(66) (67).

Differences in experimental protocols143 or interferences with the base sealer constituents (66) may be to blame for conflicting outcomes between investigations (67).

Furthermore, while adding QPEI nanoparticles to existing root canal sealers may bring a variety of advantages, it's also vital to examine the nanomaterial's potential downsides, such as polymerization shrinkage, solvent sorption, altered mechanical properties, and so on.

A study demonstrated that a new endodontic sealer using AgNPs and Dimethylaminohexadecyl methacrylate (DMAHDM) had promising antibiofilm efficacy against E. faecalis (69).

An experimental sealer containing amorphous calcium phosphate nanoparticles and DMAHDM was found to have antibiofilm activity as well as high levels of calcium and phosphate ion release, implying that it has the potential to promote remineralization and strengthen compromised root structures(70),(71) (72).

Aside from developing experimental sealers, another study used DMAHDM and AgNPs to improve and extend the antibacterial capabilities of an existing epoxy resin-based sealer. The modified sealer preserved its antibacterial capabilities for up to 14 days, but AH PlusTM lost its antibacterial efficiency by day 7. (73).

Nanostructured Silver Vanadate with AgNPs

AgNPs, as previously stated, have powerful antibacterial effects. Nanostructured silver vanadate has been suggested as a way to stabilize AgNPs(74) to enhance their potential applicability as endodontic sealers (75).

Endodontic sealers containing nanostructured silver vanadate with AgNPs appeared to have no negative effects on the physicochemical qualities (76). However, studies on its effects on sealers' antimicrobial activity have yielded contradictory findings. One study found no additional antibacterial advantage when the sealers were freshly combined, while another found that antibacterial characteristics were improved in both freshly mixed and set phases.

More clinically relevant trials, such as cytotoxicity and tooth discoloration, should be conducted to determine the degree of the benefits vs the costs (78).

Zinc Oxide Nanoparticles

ZnONPs have been employed to develop new endodontic sealers and to improve the physicochemical and antibacterial qualities of conventional zinc oxide eugenol sealers (79).

One of the earliest research used ZnONPs in a zinc oxide eugenol-based sealant, with or without chitosan nanoparticles, and found that it increased antibacterial characteristics (80).

When compared with AH 26TM and micro-zinc oxide eugenol sealer, obturation with gutta-percha and nano-zinc oxide eugenol sealer resulted in less apical microleakage (79). Nano-zinc oxide eugenol sealer was found to have no more harmful effects than other commercially available sealers like AH 26TM and PulpdentTM (81).

Versiani et al. experimented with varying concentrations of ZnONPs in a zinc oxide eugenol sealer and discovered that replacing 25% of the zinc oxide powder with ZnONPs resulted in a better seal.

Chitosan Nanoparticles

As previously stated, chitosan nanoparticles are altered by time and contact. These nano-biopolymers have the potential to be used to create new antibacterial endodontic sealers(31),(83) (84).

Several studies have looked into the possibilities of incorporating chitosan nanoparticles to increase the antibacterial and antibiofilm efficacy of conventional zinc oxide eugenol sealers (84).

The antibiofilm efficiency of a calcium hydroxide-based sealer, ApexitPlusTM, was increased by combining chitosan nanoparticles and ZnONPs, but only the sealer modified with ZnONPs was effective against the endodontic isolate strain of E. faecalis (85).

The addition of chitosan nanoparticles to ThermaSealPlusTM, an epoxy resin-based sealer, was found to improve its antibacterial activity (86). When MTA fillapexTM, a calcium silicate-based sealant, was used, however, the same level of improvement was not seen (86).

The varied physicochemical features of different sealers may interfere with or decrease any additional antibacterial benefit from chitosan nanoparticles, which could explain the varying results. (86).

Other Nanoparticle-Based Modifications of Sealers and Obturation Materials
Antimicrobial effects were shown in an experimental root canal sealer containing propolis-loaded PLGA nanoparticles against E. faecalis, Streptococcus mutans, and Candida albicans (87).

The use of doxycycline-functionalized PolymP-n Active nanoparticles to occlude dentinal tubules and provide antibiofilm actions against E. faecalis was recently discovered (88).

Bioactive glass and hydroxyapatite nanoparticles were reported to improve the bioactivity of an epoxy resin-based sealant in one investigation (89).

Finally, nanoparticulate alterations to gutta-percha have been studied in various investigations. An in vitro study found that nanodiamond-embedded gutta-percha functionalized with amoxicillin gave this hitherto inert obturation material antibacterial characteristics (90).

Following that, a clinical trial used nanodiamond-embedded gutta-percha to obturate the middle third of root canals and found no harmful effects or differences in healing outcome over 6 months when compared to the control group (91).

More research is needed to discover the ideal concentration and customize the synthesis of nanoparticle-based obturation materials so that they can give adequate antibacterial efficacy while maintaining their physicochemical features.

Regenerative Endodontic Strategies
Regenerative therapy aims to restore the form and function of a tooth by eliminating infection, promoting the development and closure of immature root apices, and re-establishing pulpal vitality. Regenerative endodontics is based on tissue engineering and biological techniques including stem cells, bioactive compounds, and scaffolds.

Nanoparticle-based carrier systems have been presented as a mechanism for the prolonged release of bioactive chemicals, which are important in regenerative endodontics because they control cellular activities such as proliferation, migration, and differentiation (94).

The vitality of stem cells from the apical papilla (SCAP) and alkaline phosphatase activity was reported to be improved by bovine serum albumin-loaded chitosan nanoparticles (95).

SCAP odontogenic differentiation was improved by dexamethasone-loaded chitosan nanoparticles (96). Dentine conditioning with chitosan nanoparticles or dexamethasone-modified chitosan nanoparticles has the potential to reduce the negative effects of NaOCl and LPS while also increasing SCAP adherence, survival, and differentiation. 179,182

Bellamy et al. found that a carboxymethyl chitosan-based scaffold containing transforming growth factor-1-loaded chitosan nanoparticles improved SCAP viability, differentiation, and migration (97).

The inclusion of dexamethasone and bioactive glass nanoparticles into a nanofiber scaffold system has also been shown to enhance the odontogenic differentiation of human dental pulp cells (97). The addition of bioactive glass nanoparticles to scaffolds may improve mechanical characteristics while also encouraging bioactivity and mineralization through calcium release and deposition (98).

Another study reinforced hydrogel scaffolds using cellulose nanocrystals, resulting in enhanced stiffness and stability. Platelet lysate, which is high in proangiogenic and chemotactic factors and has the potential to improve pulpal tissue revascularization and regeneration, was also added to the reinforced hydrogel (99).

Biz et al combined gold nanoparticles with L-lysine, a biodegradable organic material, to make compounds that stem cells could easily absorb. The researchers discovered that the increased radiopacity of the cells could allow microtomography to identify the existence of live cells after regeneration operations with no obvious harmful consequences (100).

Conclusion:-

Nanotechnology creates incredibly useful structures from individual atoms or molecules, which provides an alternative or possibly superior approach in designing and application of nanomaterials in endodontics. Owing to the advantages and applications explained, they are largely in a conceptual stage, but at the outset, we can foresee that there will be translation into the clinical applications as well. The era of nanotechnology has dawned. This is the prevailing research field, which helps us to introspect and discover the universe within ourselves.

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