Role of Nanotechnology in Dental Decay: A Review

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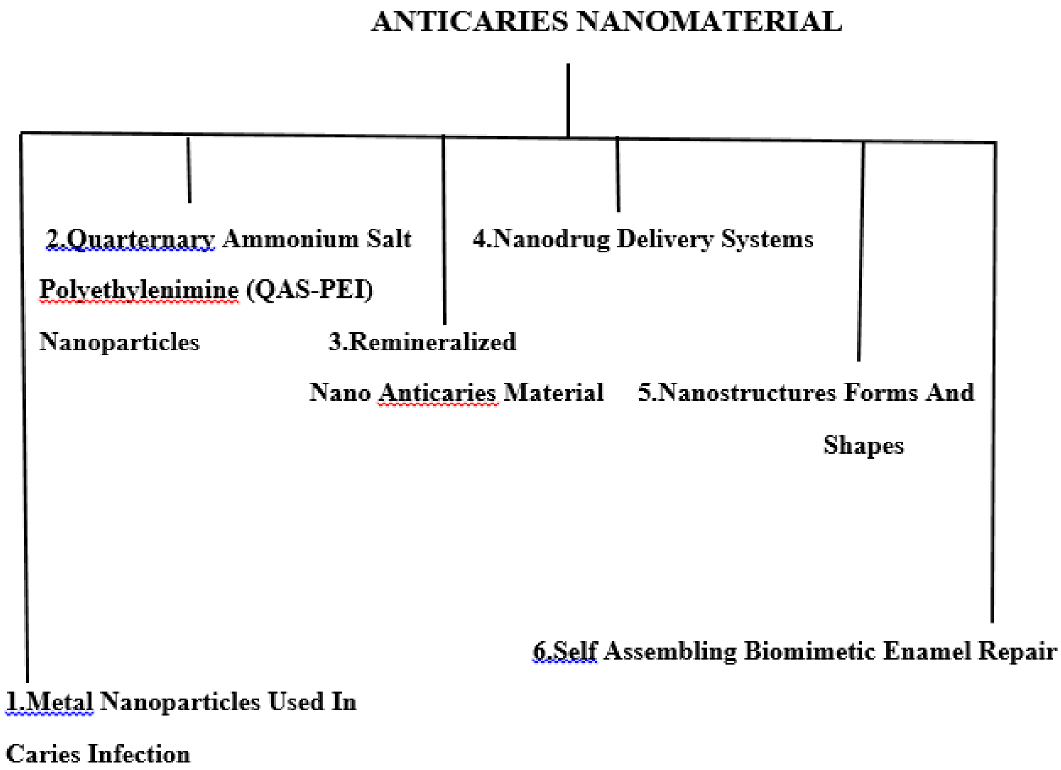
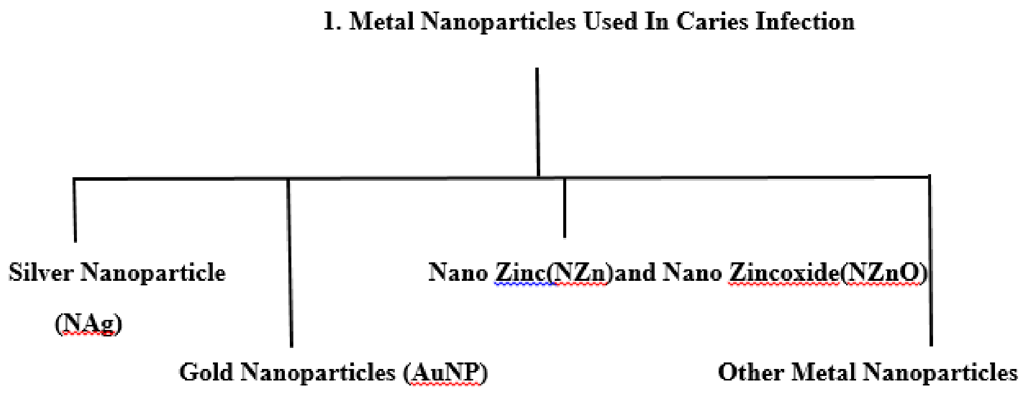
Abstract Dental caries (tooth decay) is probably the most common chronic diseases in the world. Lack of anti-caries properties in traditional caries filling materials can result in secondary caries and treatment failure. The invention of nanotechnology in dental caries is an effective strategy for caries management because the bacterial metabolism gets interfered, the formation of biofilm gets inhibited, demineralization gets reduced, and remineralization gets promoted, which is the reason why it is in the pioneer role. In this review article we have tried covering all the aspects and types of nanomaterials that will be useful for our budding and experienced dentists worldwide in anticaries management.
Keywords: Metal nanoparticle, QAS-PEI, Remineralized Nano Anticaries Material, Nanostructures Forms and Shapes, Nanodrug delivery system, Self-Assembling Biomimetic Enamel Repair

INTRODUCTION

Dental Caries is an infectious microbiologic disease of the teeth which causes the calcified tissues to undergo dissolution and destruction. Collection of microorganisms where the cells adhere to each other as well as to the tooth surface[1] is called as biofilm. These biofilm of oral bacteria and yeast leads to several localized disease in the oral cavity including dental caries, periodontal diseases, candidiasis and endodontic, orthodontic and implant infections[1].Complex interaction between acid producing bacteria and host factors including teeth and saliva[2] leads to caries formation. Based on modern theory of caries etiology, imbalance of oral flora could result in acid accumulation and lead to tooth demineralization[3].The initial colonizers at first sticks to the acquired pellicle which is a salivary- dietary- derived proteinaceous layer present on the tooth surface that subsequently influences the further colonization of microbial organisms[1]. As a result, dental plaque is formed and its maturation is characterized by bacterial interactions such as **Co-aggregation** and **Quarum Sensoring** and increasingly diverse bacterial populations[2].Acids as by products are being produced by these bacterial species from the metabolism of fermentable carbohydrates resulting in demineralization below the tooth surface.

Richard Feynman first proposed nanotechnology. It is a technology that is based on the properties and application of materials in the range of 1-100nm.Their physical/chemical advantages for eg: volume effect, surface effect, quantum size, quantum tunnel and dielectric confinement[3]makes them better than the traditional materials. The diameter of nanoparticles is inversely proportional to its specific surface area, mechanical properties and antibacterial effect. In simpler words more smaller the diameter of nanoparticles greater will be its specific surface area and stronger will be its mechanical properties and antibacterial effect[3].Nanoparticles can be used as the carrier of antibacterial drugs since they have the properties of targeting bacteria with least side effects on the host. To say about the antibacterial mechanism of nanoparticles, it includes metal ion release, oxidative stress and non oxidative mechanism[3].The positively charged nanoparticle comes in contact with negatively charged bacterial cell membrane by static electricity which changes the permeability of cell wall leading to rapture of cell membrane and organelle leakage.





4. Nano Drug Delivery Systems

i) Mesoporous Silica Nanoparticle(MSN)
ii) Aluminosilicate Clay nanotubes
iii) Reactive nanogel Adhesives
iv) Liposomes
v) Polyamidoamine (PAMAM)
vi) Halloysite NanoTube (HNT)
vii) Dental Caries Vaccine

1. Metal Nanoparticles Used in Caries Infection

Metals has been used for centuries as antimicrobial agents. Silver, Copper, Gold, Titanium, and zinc have attracted particular attention, each having different properties and spectra of activity.

With respect to nanoparticles, the antimicrobial properties of silver (Sondi and Salopek-Sondi,2004) and copper (Cioffi et al, 2005) have received the most attention. Both of these have been coated onto or incorporated into various materials (Li et al,2006), including PMMA (Boldyryeva et al,2005) and hydrogels (lee and Tsao,2006).An inverse relationship between nanoparticle size and antimicrobial activity has been demonstrated, where nanoparticles in the size range of 1 -10nm have been shown to have the greatest biocidal activity against bacteria (Morone et al,2005;Verran et al, 2007).Nanoparticles also offers advantages to the biomedical field because of their improved biocompatibility (Kim et al, 2007)due to their small size. Also, bacteria acquires more resistance against conventional and narrow-target antibiotics (Pal et al, 2007) than metal nanoparticles. This is thought to occur because metals may act on a broad range of microbial targets, and many mutations would have to occur for microorganisms to resist their antimicrobial activity.

The Anti - Caries Mechanism Of Metal Nanoparticles

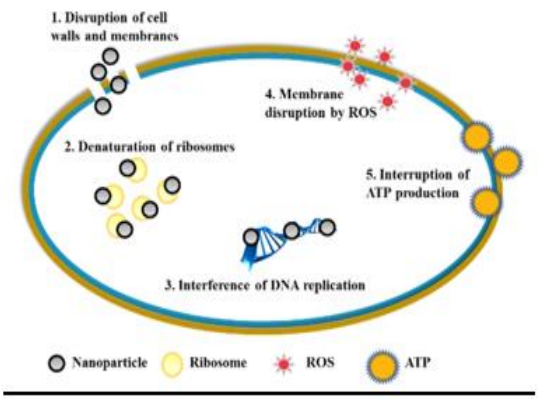


Fig1: The antibacterial mechanism of metal nanoparticle

A. Silver nanoparticle

Silver has a broad spectrum of antibacterial properties, which can inactivate enzymes and prevent DNA replication in bacteria. Surface area ratio is further increased by NAg, which makes the silver particles smaller and antibacterial effects better. According to some study, the antibacterial effect of NAg increases in a dose dependent manner from 0.05%-0.1% without any effect on bonding strength or color. Self-etching adhesive[4] containing 0.05%-0.1% NAg can affect the bonding strength at ph 2.7 according to Elkaas DW et al. Based on a study done by Cheng et al[5] 0%- 0.175% of NAg composite resin can remarkably deminish biofilm growth and metabolic activity, in which antibacterial activity shoots up in a dose - dependent manner. But, the nano- silver mass fraction was more than 0.175%[6] when the flexural strength of modified composite resin decreased significantly

Antibacterial Activity of Silver nanoparticle

Nanoparticles are now considered a viable alternative to antibiotics and seem to have a high potential to solve the problem of the emergence of bacterial multidrug resistance[7]. Silver has always been used against various diseases; in the past it has been used as an antiseptic and antimicrobial against Gram-positive and Gram-negative bacteria due to its low cytotoxicity[8]. AgNPs were considered, in recent years, particularly attractive for the production of a new class of antimicrobials, opening up a completely new way to combat a wide range of bacterial pathogens.

Details of AgNPs and their mechanisms of action against Bacteria and biofilm

Bacteria	Mechanism Of Action
Acinetobacter baumannii	Alteration of cell wall and cytoplasm.
Escherichia coli	Alteration of membrane permeability and respiration
Enterococcus faecalis	Alteration of cell wall and cytoplasm
Klebsiella pneumoniae	Alteration of membrane
Listeria monocytogenes	Morphological changes, separation of the cytoplasmic membrane from the cell wall, plasmolysis
Micrococcus luteus	Alteration of membrane
Nitrifying bacteria	Inhibits respiratory activity
Pseudomonas aeruginosa	Irreversible damage on bacterial cells; Alteration of membrane permeability and respiration
Proteus mirabilis	Alteration of cell wall and cytoplasm.
Staphylococcus aureus	Irreversible damage on bacterial cells
Staphylococcus epidermidis	Inhibition of bacterial DNA replication, bacterial cytoplasm membranes damage, modification of intracellular ATP levels
Salmonella typhi	Inhibition of bacterial DNA replication, bacterial cytoplasm membranes damage, modification of intracellular ATP levels
Vibrio cholera	Alteration of membrane permeability and respiration

B. Gold Nanoparticle (AuNP)

Gold shows a weak antimicrobial effect in comparison with silver and copper[9]. However, gold nanoparticles are employed in multiple applications involving biological systems. The binding properties of gold are exceptional and this makes it particularly suitable for attaching ligands to enhance biomolecular interactions. Gold nanoparticles also exhibit an intense colour in the visible range and contrast strongly for imaging by electron microscopy[10].

C. NanoZinc (NZn) And NanoZincoxide (NZnO)

The antibacterial ability of NZn results from the quantum size effect of dissolving and releasing zinc nanoparticles[11] and that is why it has a wide antibacterial spectrum. NZn has the property of reducing the expression of MMPs and increase the lifespan of adhesive[12]. Based on a study the addition of Zn^{2+} to total-etch adhesive can result in inhibition of MMP activity, reduction in the decomposition of dentin collagen bundle, and protection of mineral crystal formation at the eosin–tooth interface, which will result in improvement of the nano-mechanical properties[13].

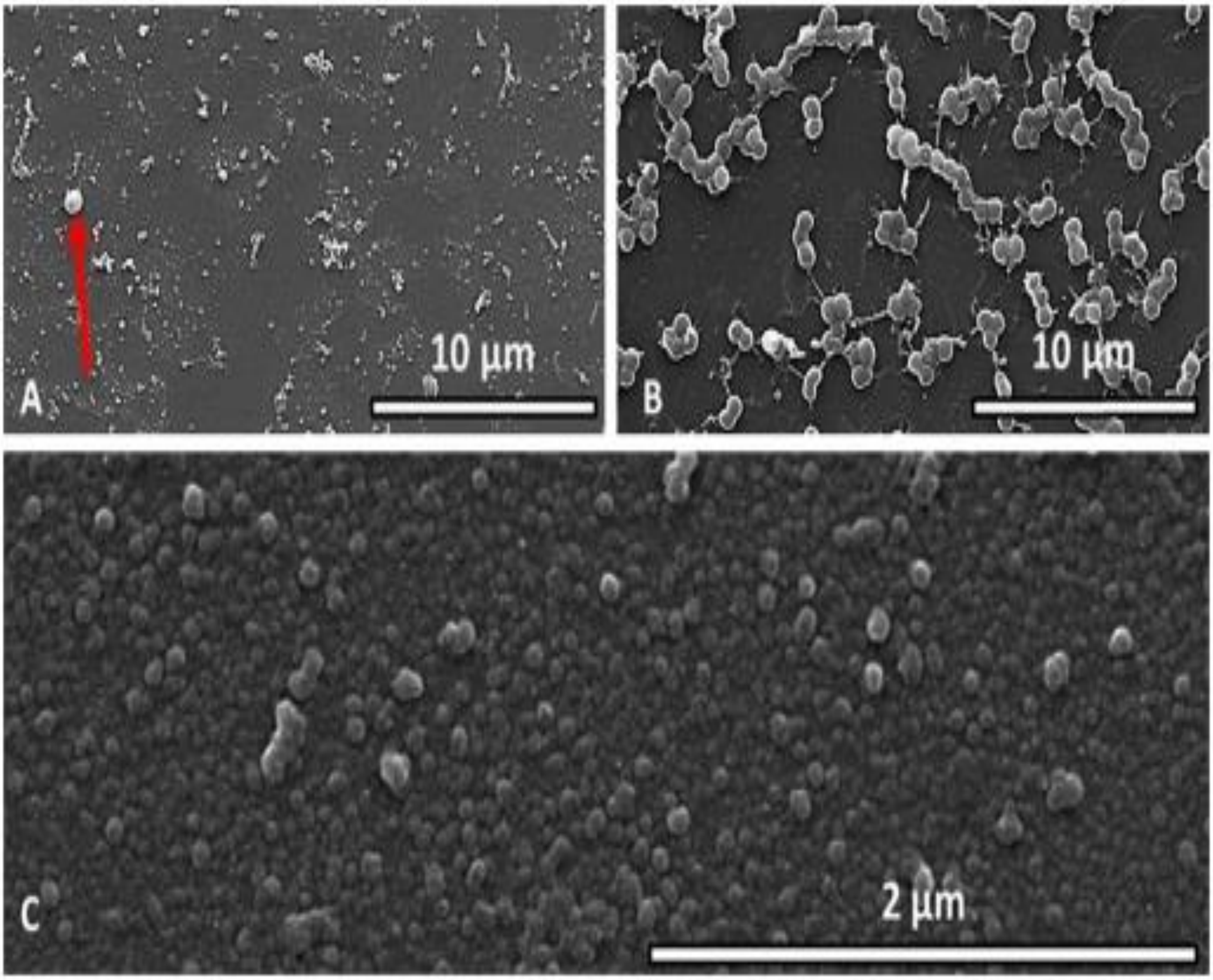


Fig 2: Assessment of the bactericidal effect of nanoparticulate ZnO-coated glass substrates. (A) Arrow indicates an individual Staphylococcus aureus cell present on the coated surface. Debris present is likely to be remnants of dead bacteria. (B) A population of S. aureus present on an untreated surface. (C) High-resolution image to highlight the uniformity of the coated surface

2. Quarternary Ammonium Salt Polyethylenimine (QAS-PEI) Nanoparticles

QAS is a highly active cationic agent with a wide antibacterial spectrum[14]. Based on the polyethylenimine cross-linked structure, QAS-PEI nanoparticles were prepared making the modified composite bear the property of high chemical stability and antibacterial properties under different oxidants and storage conditions, without the oral micro ecological balance[3]getting effected. QAS-PEI has the antibacterial mechanism based on the electrostatic interaction between QAS-PEI which is positively charged and bacterial cell walls[15]which is negatively charged.

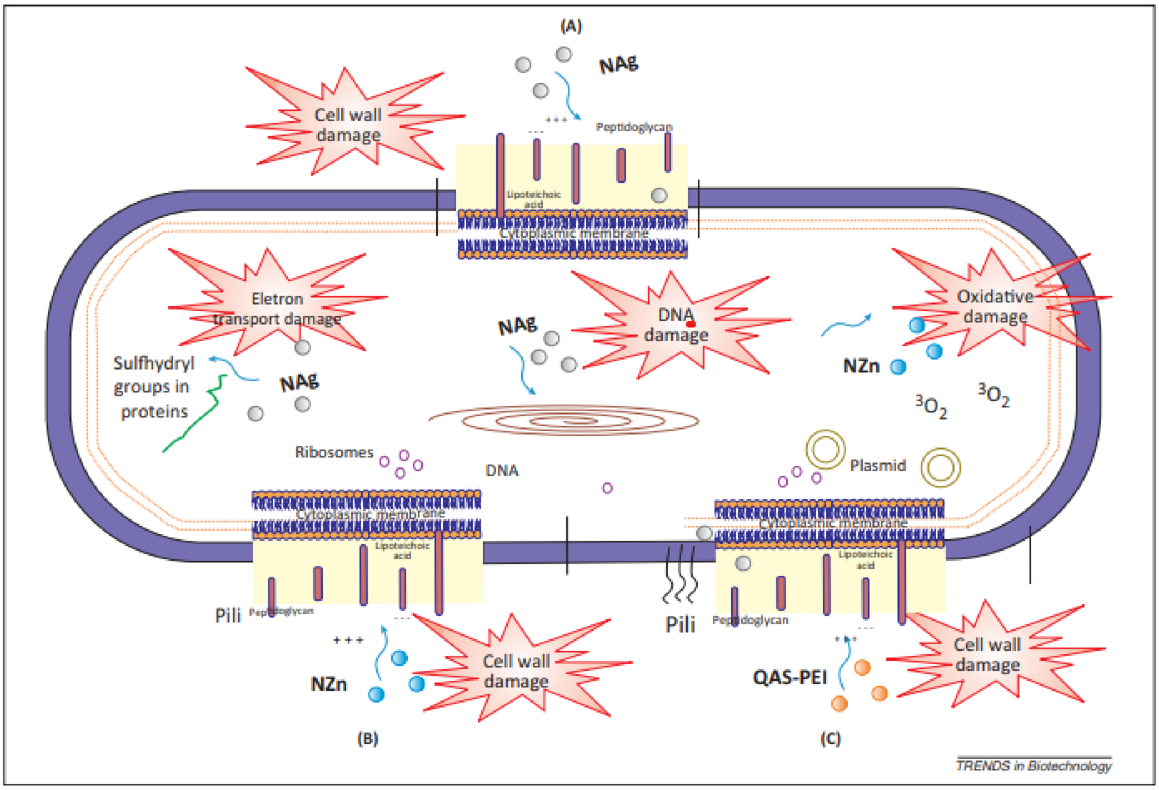


Fig 3: Schematic representation of a bacterial cell showing the components targeted by different antibacterial agents incorporated in dental materials. (A) Silver nanoparticles (NAg): NAg have been incorporated in restorative materials to combat the cariogenic bacteria colonization in the marginal gaps and on their surfaces. (B) Zinc oxide nanoparticles (NZn): the primary cause of the antibacterial function of NZn is credited to the disruption of cell membrane activity. (C) Quaternary ammonium polyethylenimine (QAS-PEI) nanoparticles: the mechanism of action may be related to absorption of positively charged polymers onto negatively charged cell surfaces of the bacteria. This process is thought to be responsible for the increase of cell permeability and may disrupt the cell membranes.

3. Remineralized Nano Anticaries Material

Multiple innovative applications of nanotechnology have been postulated in the aim of attaining net remineralization of early caries lesions as a non-invasive approach for dental caries management[6]. The remineralization procedure confers the provision of calcium and phosphorous ions from an external source to the dental structures in order to enhance ion precipitation into the demineralized surface to earn lucid remineralization and furnish anti-cariogenic effect.

4. Nano Drug Delivery Systems

i) Mesoporous Silica Nanoparticle (MSNs):

The surface of MSN can be modified by functional groups resulting in MSN being compatible with various solutions and it can also be stored as different types of molecules[3]. Other than that MSN is easy to adhere to the dentin surface because of its high affinity. MSN can also release calcium and phosphate slowly leading to the improvement of the bonding durability and remineralization effect.

ii) Aluminosilicae Clay nanotubes:

Aluminosilicate ($Al_2Si_2O_5(OH)_4 \cdot nH_2O$) clay nanotubes (Halloysite, HNT) have many advantages (e.g., biocompatibility, hydrophilicity, and high mechanical strength) that make them a good candidate to be used as a reinforcing agent for improving resin-based dental adhesive properties[6]. Besides, these clay nanotubes can also behave as biologically safe reservoirs leading to the encapsulation and controlled delivery of a wide variety of therapeutics. In adhesive dentistry, these nanotubes can be a carrier of MMP inhibitors, that would ultimately result in reducing and/or eliminating resin–dentin bond degradation.

iii) Reactive nanogel Adhesives

Nano-gels are 10- to 100-nm cross-linked globular particles synthesized through a versatile route allowing for adjustable hydrophobic character and level of methacrylate functionalization[6]. Nano-gels can be swollen by and dispersed in monomers such as BisGMA, HEMA and solvents, which, in dentin bonding, are anticipated to carry the nanoparticles into demineralized dentin.

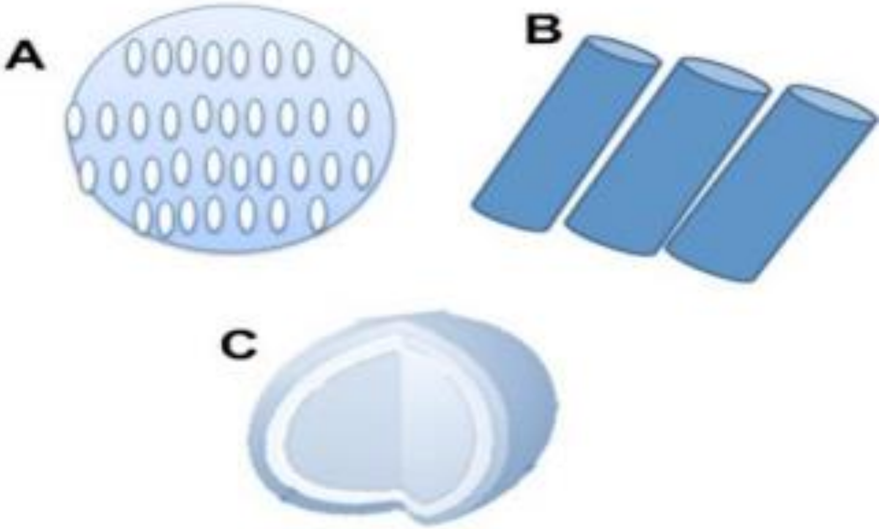


Fig 4: Schematic diagram representing different patterns of drug carriers nanoparticles; A: Mesoporous spherical nanoparticle, B: Nanotube, C: polymeric Nanocarrier.

iv) Liposomes

A liposome is a microvesicle formed by encapsulating drugs in the lipid bilayer[3]. Liposomes were used as a drug carriers for the first time by Gregoriadis et al. Lipophilic or water-soluble drugs can be encapsulated by liposomes which possesses the properties of anti-cancer, antibacterial, anti-inflammatory drug carriers along with gene delivery because it has an additional advantage of targeting, slow-released and tissue affinity after encapsulating drugs. The anticaries role of liposomes is mainly described by liposome drug delivery system which is actually the source of calcium, phosphorus, and other minerals being precipitated on the surface of tooth hard tissue promoting mineralization.

Liposomes containing fat-soluble or water-soluble antimicrobial agents can diminish plaque biofilms as well.

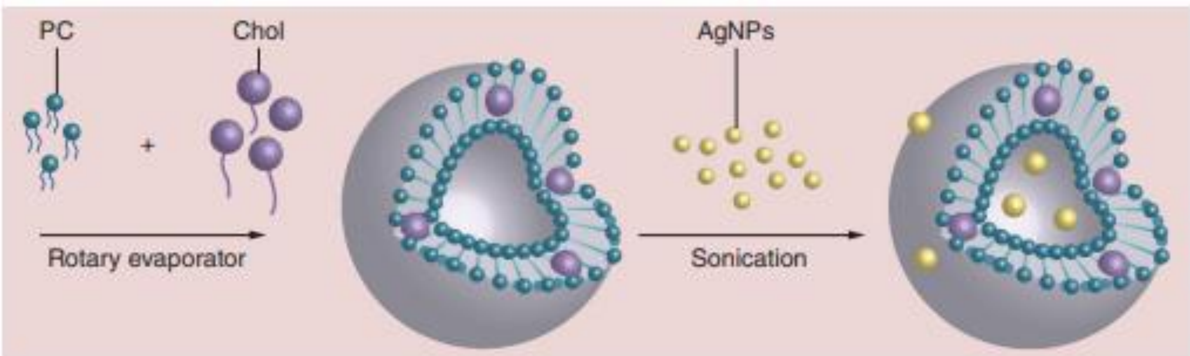


Fig 5: Synthesis of liposome silver nanoparticles

v) Halloysite Nano-Tube (HNT)

Halloysite is a kind of natural silicate mineral, which mainly exists in nature in the form of nanotubes[3]. The main role of HNT is that it acts as a carrier to regulate the delivery of therapeutic agents along with excellent biocompatibility, hydrophilicity, and high mechanical strength.

vi) Polyamidoamine(PAMAM)

A dendrimer is a novel type of high branched nano polymer with a cavity in the molecule and easy to modify surface groups[3]. It possesses the property of excellent biocompatibility, reduced toxicity, and non-immunogenicity. Modification of PAMAM terminal groups into various functional groups as drug delivery carriers can result in controlling release of the drug and act as both antibacterial and remineralization in caries.

vii) Dental Caries Vaccine

It is an effective strategy in caries prevention to induce oral mucosal immune systems through the nasal tract[3]. Vaccination carries the following advantages of greater patient compliance, induces systemic immunity, and administration is convenient.

5) Nanostructures Forms and Shapes

Nanostructures comes in different forms and shape having dimensions in the range between 0.1-100 nm[6]. They are made up of different compositions, and resulting in greater variety of modified properties to enable innovative applications in dentistry

6) Self Assembling Biomimetic Enamel Repair

Dental enamel represents a unique hard biological tissue yet, incapable to repair when subjected to acid dissolution under the effect of caries activity followed by ulterior collapse of its organic construction yielding cavity formation. The non-regenerative phenomenon arises as a result of being devoid of vital cellular component lost soon after tooth emergence into the oral cavity[6]. Biomimicry approaches for enamel repair rely on bio-mineralization to enhance artificial enamel formation in attempt to reform surface damage

CONCLUSION

With the development of caries diagnosis and prevention, nanotechnology will significantly improve medical treatment. The application of nanoparticles against caries infection is very important because it has antibacterial, remineralization, and drug loading capacity. This review article highlights that nanoparticles have innumerable role in the prevention and treatment of dental caries. However, their disadvantages and potential cytotoxicity and environmental effects cannot be neglected. In the coming days, we should focus on discovering better and modern technology to develop highly effective anti-caries nanoparticles along with highest safety for patients. Further studies about nanotechnology in dental caries prevention and management are needed.

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