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Review Article

ADVANCED APPROACHES OF POLYSACCHARIDE FUNCTIONALIZED SILVER NANOPARTICLES IN DENTAL APPLICATIONS: A CRITICAL REVIEW

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ABSTRACT

Silver nanoparticles (AgNPs) have become an integral part of modern dentistry as they are highly antimicrobial. Recent studies involving the green synthesis of AgNPs from polysaccharides have opened up new prospects for enhancing the efficiency and safety of AgNPs. This review aims to explore novel directions with AgNPs polysaccharide systems through their synthesis, engineering, characterization, and dental applications. The scientific articles published between 2012 and 2024 in different journals were downloaded from PubMed, Science Direct platforms, and Google Scholar profiles to complete the current review after filtering out non-qualifying articles. The diagrams were prepared manually using online software. This study unfolds the novel applications of polymer-conjugated AgNPs as next-generation antimicrobial agents, offering an additive approach for combating resistant microbial infections. Polysaccharide matrices stabilize AgNPs, optimizing their bioavailability and targeted biofilm disruption. Comparative studies show that AgNP-conjugated systems surpass unmodified counterparts in *Streptococcus mutans* for elimination of biofilm and preventing demineralization of enamel through prolonged ion release and augmented mucosal adhesion. Integrating polysaccharide-functionalized AgNPs in dental applications represents a significant advancement, offering enhanced antimicrobial efficacy while mitigating toxicity concerns. Comparative analyses highlight superior antimicrobial activity against *S. mutans* compared to unmodified AgNPs. Therefore, future research should focus on exploring natural polysaccharides for standardizing synthesis protocols of polysaccharide-AgNPs hybrids to ensure reproducibility and safety for preventing oral infections and promoting oral health, underscoring the need for rigorous clinical trials to validate their long-term efficacy and safety.

Keywords: Silver nanoparticles, Polysaccharide, Dental application, Antimicrobial, Synthesis.

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INTRODUCTION

In recent era, most of the non-communicable diseases of oral cavity such as dental caries and periodontal diseases are significantly impacting health due to microbial activity. Dental caries arises from the demineralization of tooth structure caused by acid-producing bacteria, while periodontal diseases stem from inflammatory responses to bacterial biofilms on teeth and gums The complexity of dental diseases is depicted in Fig. 1. Chlorhexidine mouth rinses, fluoride varnishes, gels, and restorative materials are examples of currently marketed dental disease management treatments. While these medications reduce plaque and gingivitis, they might have adverse effects such as discoloration and cellular damage, emphasizing the need for novel remedies [1].

The nanoparticle (NPs) technology utilization had distinctive characteristics for tailored delivery, including elevated surface area-to-volume ratio and potential drug release characteristics. These nanomaterials have contributed significantly to different experimental dental uses by integrating into materials such as metals, resin, and ceramics employed as restorative, endodontics, periodontal treatment, prosthetic, and implants to cure oral diseases. From numerous nanomaterials available, silver NPs (AgNPs) are becoming increasingly crucial in dental uses because of their potent antimicrobial activity and capacity to increase the efficacy of other therapeutic agents [2,3].

Apart from that, natural polymers with antioxidant and antimicrobial activity are also entering into competition with AgNPs, either resulting in green synthesized AgNPs or can be used to develop polymer functionalized AgNPs. Cifuentes-Jiménez *et al*. (2024) have successfully green synthesized *Camellia sinensis* derived AgNPs and functionalized them with chitosan and fluoride, resulting in an additive activity of AgNPs with chitosan in treating dental caries and causing remineralization and strengthening of dentine [4].

The integration of polysaccharides facilitates the prolonged release of AgNPs, reducing application frequency while maintaining efficacy against microbial infections. A recent study by Ismail *et al*. synthesized green palladium NPs with polyvinyl alcohol or alginate hybrid scaffold composites. The result confirmed the remarkable mechanical properties of formulation with good osteogenic differentiation capacity, enhancing osteoconductive properties [5].

The present review focuses on innovative approaches to combat dental diseases, mainly through the implications of polysaccharides in NPs, which may provide a promising frontier in oral health management. Future research should focus on optimizing formulation and delivery mechanisms of these nanomaterials in dental products to enhance their therapeutic effects and pave a new way for more effective, sustainable, and patient-friendly formulations globally.

NPS IN DENTAL APPLICATIONS

Nanotechnology is revolutionizing dental medicine by developing innovative nanosystems, including NPs and nanostructured materials. By leveraging these nanomaterials' intrinsic characteristics and biological properties, dental applications can enhance therapeutic outcomes, improve diagnostic capabilities, and facilitate targeted drug delivery [6,7]. AgNPs may be synthesized by various techniques as per Fig. 2, broadly categorized into chemical, physical, and biological methods [8]. Mechanism of action of AgNPs in microbial cell is depicted in Fig. 3 and Table 1 lists the various types of NPs explicitly used in dental treatment.

Different application forms of NPs [33,34]

Gels

NPs-infused gels are utilized for their antimicrobial properties and enhanced delivery of therapeutic agents. These gels can be applied directly

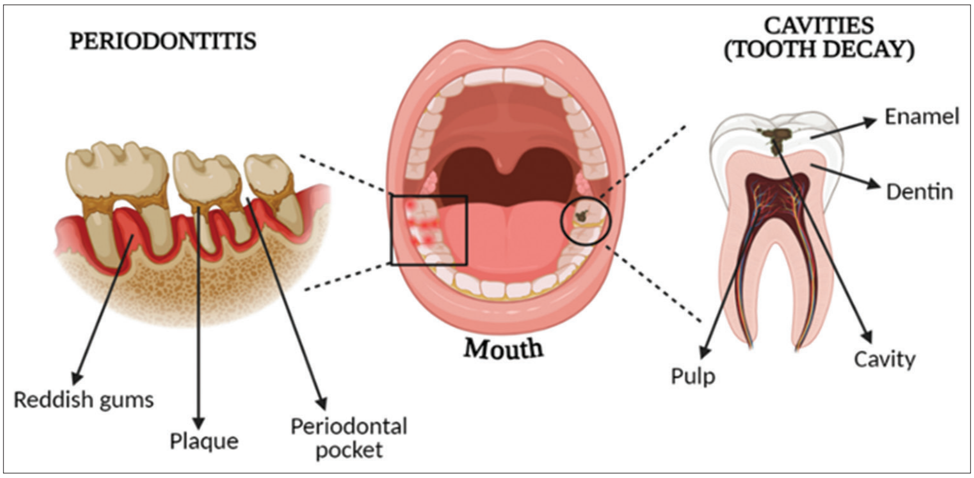

Fig. 1: Representation of different dental diseases

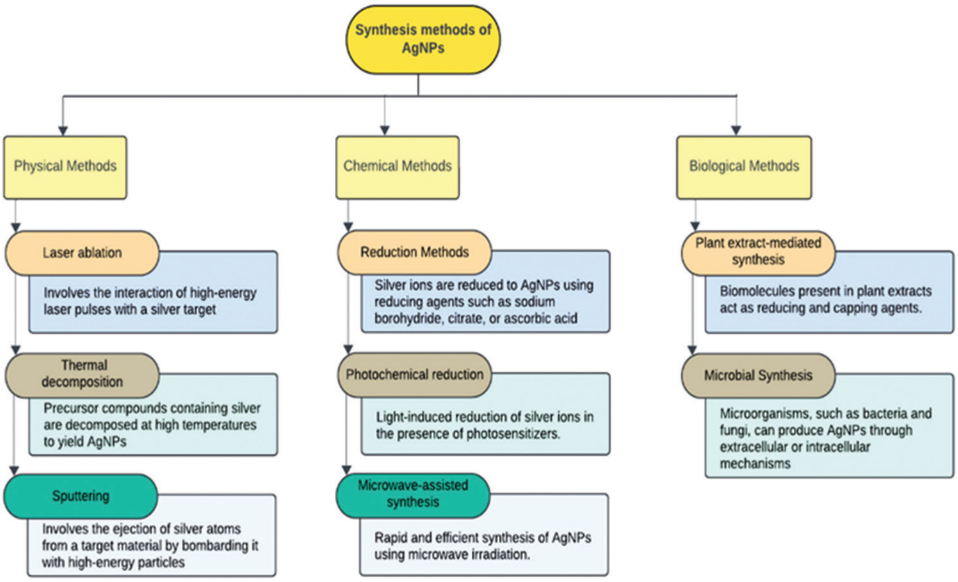

Fig. 2: Schematic diagram representing synthesis methods of silver nanoparticles

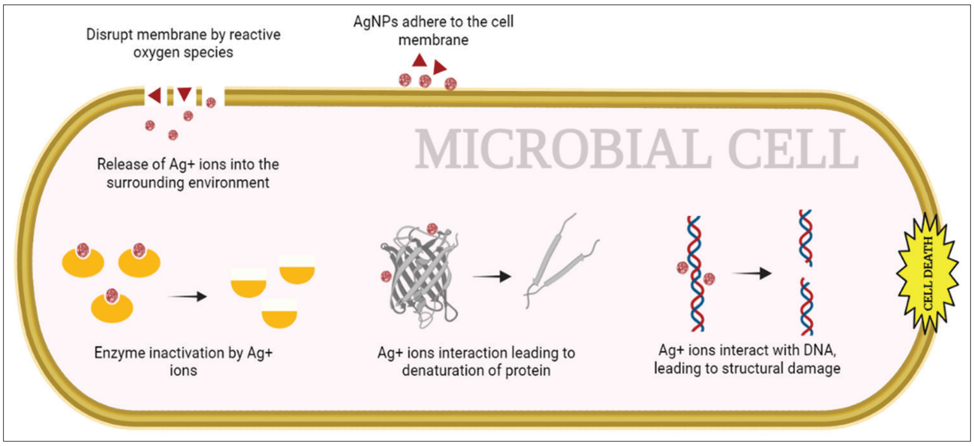

Fig. 3: Mechanism of silver nanoparticles against microbial cell

to the affected areas, promoting localized treatment with a decrease in the systemic side effects of drugs. For instance, zinc oxide NPs incorporated into dental gels have shown significant antibacterial effects against *Streptococcus mutans*. The application of NPs in oral cavity is depicted in Fig. 4.

Implants

Dental implants are prosthodontic restorations offered through surgical procedures that are placed within the jawbone to serve as artificial roots to hold artificial teeth. Titanium dioxide (TiO_2)

Table 1: Nanoparticles in dental treatments

Sl. No.	NPs	Dosage form	Synthesis method	Therapeutic effects	References
1.	Silica nanoparticles (SNPs)	Gel form	Stober synthesis method	Improved microhardness, fracture toughness, and flexural strength in tooth	Pavanello *et al.* [9]
2.	Zirconium dioxide NPs (nano-ZrO_2)	Dental resin	Silanized and surface-treated before use	Improved the resin elastic modulus for dental restorations and flexural strength	Almedarham *et al.* [10]
3.	Carbon-based nanomaterial (Pyrolytic carbon)	Implants coating	Thermal spraying or depositing hydrocarbons	Improved osseointegration	Maher *et al.* [11]
4.	Carbon nanotubes (CNTs)	Dental cement	Electric arc discharge, laser ablation	Modified the dentin surface and dental bonding	Maher *et al.* [11]
5.	Mesoporous Calcium Silicate Nanoparticles (MCSNs)	Powders	Template method	Showed low cytotoxicity and high antibacterial potency against *Enterococcus faecalis*, particularly in endodontics therapy	Mohammed and Ali [12]
6.	Metal nanoparticles (MNPs)	Toothpaste, mouthwash, and dental cement	Green synthesis from *Salacia chinensis*	Promoted bone regeneration	Yazdanian *et al.* [13]
7.	Metal nanoparticles and metal oxide nanoparticles	Endodontic sealers, irrigants, and intracanal medicaments.	Green synthesis, physical and chemical methods	Improved mechanical integrity of dental materials and potential for tissue regeneration in endodontic treatments	Sharifi *et al.* [14]
8.	Aluminum oxide (Al_2O_3) nanoparticles	PMMA composites	Sol-gel technique and employed to incorporate hybrid fillers of Al2O3 into the PMMA resin	Enhanced mechanical strength of the PMMA composite and improved wear resistance	Nabhan *et al.* [15]
9.	Graphene nanoparticles	Graphene-doped materials for dental implants	Chemical vapor deposition, liquid phase, and mechanical exfoliation	Improved osseointegration, reduce inflammation, promote tissue regeneration	Mobarak *et al.* [16]
10.	Chlorhexidine-loaded silica nanoparticles (SNPs)	Dental composites	Stöber method and coated with the Layer-by-Layer (LbL) technique	Showed significant antimicrobial activity against *Streptococcus* species and reduced biofilm formation.	Larissa *et al.* [17]
11.	Cerium oxide nanoparticles (CeO_2NPs)	Restorative cements/ sealants	Chemical synthesis (e.g., precipitation, solvothermal, sol-gel, microemulsion)	Exhibited antioxidant, antibacterial, and anti-inflammatory properties, effective in preventing dental caries	Jairam *et al.* [18]
12.	Zirconium nanoparticles (ZrO_2)	Coatings on dental implants	Sol-gel, spinning, vapor deposition	Enhanced osseointegration, biocompatibility, and mechanical properties of dental implants	Hossain *et al.* [19]
13.	Zirconium nanoparticles (ZrO_2)	Paste	Green synthesis using ginger and garlic extracts	Showed antibacterial activity against *S. aureus* and demonstrated potential for osseointegration	Chowdhury *et al.* [20]
14.	Magnesium oxide (MgO) nanoparticles	Dental cements	Sol-gel technique and pH-controlled nanoprecipitation	Reduced bacterial colonization and decreased recurrent caries and gingival infections	Naguib *et al.* [21]
15.	Gold nanoparticles (AuNPs)	Calcium phosphate cement	Chemical Reduction Method	Enhanced osteogenic function of cells and enhanced bond regeneration	Xia *et al.* [22]
16.	Gold nanoparticles (AuNPs)	Nanoparticles	Chemical Reduction Method with aqueous leaf extract of *Anogeissus latifolia* as reducing agent	Enhanced cell viability and osteoinductive potential, suitable for dental implants.	Wang *et al.* [23]
17.	Titanium dioxide (TiO_2) nanoparticles.	Dental adhesives	Grafting from technique	Provide stronger bonds to human teeth and increased shear bond strength	Sun *et al.* [24]

(Contd...)

Table 1: *(Continued)*

Sl. No.	NPs	Dosage form	Synthesis method	Therapeutic effects	References
18.	Zinc oxide nanoparticles (ZnO-NPs)	Resin composites	Solvent-based ultrasonic irradiation	Improved antibacterial properties, mechanical behavior, and biocompatibility of dental restorative materials	Moradpoor *et al.* [25]
19.	Copper oxide nanoparticles (CuO-NPs)	Plates	Laser ablation in liquids	Strong antibacterial activity and cytocompatibility with periodontal ligament stem cells of humans	Fernández-Arias *et al.* [26]
20.	Carbamide peroxide polymeric nanoparticles	Whitening gel	Coacervation	Showed high stability and effective bleaching properties for dental whitening	Lima *et al.* [27]
21.	Boron-doped bioactive glass nanoparticles (BG-NPs)	Nanoparticles	Sol-gel method	Enhanced the early-stage odontogenic differentiation of human dental pulp stem cells (hDPSCs)	Moonesi Rad *et al.* [28]
22.	Bioactive glass nanoparticles (NBG)	Powder form	Sol-gel method	Orthopedic applications and increased mesenchymal stem cell (MSC) proliferation	Ajita *et al.* [29]
23.	Copper nanoparticles (Cu-NPs)	Dental amalgam, cements, adhesives	Chemical method	Enhanced prevention from oral infections and promote bone regeneration	Xu *et al.* [30]
24.	Gold nanoparticles (Au-NPs)	Nanoparticles	Green chemistry method	Increased cell viability and osteoinductive potential	Jadhav *et al.* [31]
25.	TiO_2 nanohybrid particles	Fillers in light-curing dental composite materials	Microwave synthesizer	Improved the mechanical strength and durability of the dental composites	Raorane *et al.* [32]

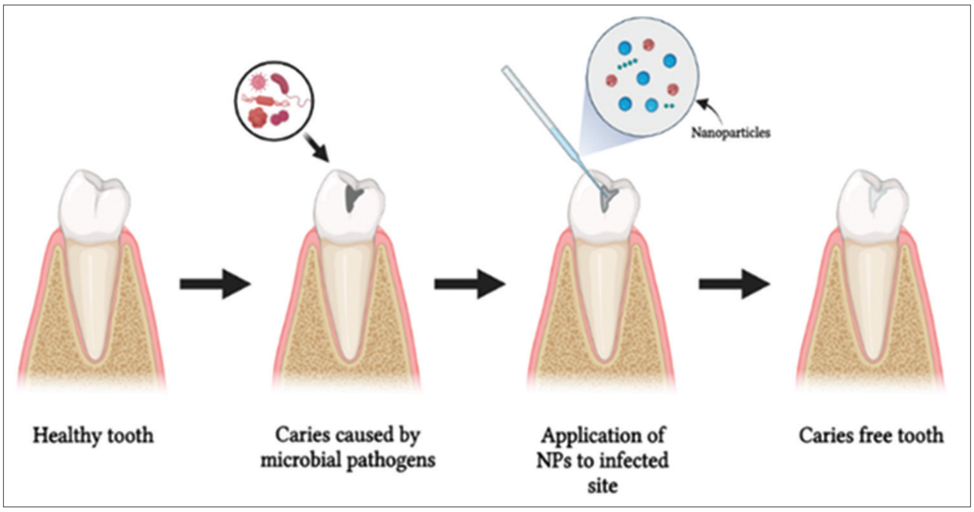

Fig. 4: Application of nanoparticles in oral cavity

NPs are commonly used to promote the osseointegration of implants. A study reveals that TiO_2 nanotubes on implant surfaces significantly enhanced bone growth and integration compared to traditional surfaces. This modification leads to better stability and longevity of dental implants, making them more effective in clinical settings.

Biofilms

AgNPs can effectively restrict biofilm growth formed by cariogenic bacteria, thereby reducing the incidence of dental caries. A case study highlighted AgNPs-coated dental materials that significantly reduced biofilm formation on composite surfaces.

Sealers

NPs-based sealers have revolutionized root canal treatments. Bio-ceramic sealer, which incorporates bioactive NPs, has been shown to possess excellent dimensional stability and antimicrobial properties. This sealer effectively fills the root canal space and promotes healing by releasing calcium silicate and hydroxyapatite upon hydration, facilitating tissue regeneration in the periapical area.

Fillers

NPs are also employed in dental composites as fillers to enhance mechanical properties and reduce wear. A study demonstrated that composites with silica NPs exhibited significantly better wear resistance and mechanical strength than conventional composites, making them suitable for high-stress applications in posterior teeth restorations.

Restorative materials

Nano-hydroxyapatite has been integrated into restorative materials to mimic the natural mineral composition of teeth. In addition to improving the mechanical properties of the materials, the incorporation enhances their biocompatibility and bioactivity so that remineralization of demineralized tooth structure can be induced.

Regenerative materials

NPs are utilized in scaffolds for tissue engineering, facilitating the reformation of dental tissues such as dentin and pulp. Research has shown that scaffolds impregnated with these NPs promote cell attachment and proliferation, leading to effective tissue regeneration in preclinical models.

Toxicities associated with AgNPs [35-37]

NPs in dental materials can cause cytotoxicity, genotoxicity, and organ damage through inhalation, ingestion, and dermal exposure. Therefore, high-efficiency particulate air filters, high-flow suction, and personal protective equipment can reduce patient exposure to NPs. Furthermore, coating the NPs with polymers or antioxidants can reduce toxicity and improve safety assessment [38].

Inflammatory responses

AgNPs have been linked to inflammatory effects in various tissues, contributing to conditions such as pulmonary inflammation.

Hepatotoxicity

Studies indicate that AgNPs can cause liver toxicity, affecting liver function and health.

Neurotoxicity

Research has shown that AgNPs are able to cross the blood–brain barrier, leading to such particle deposition in the brain and subsequent neuronal necrosis and degeneration.

Tissue distribution and accumulation

Silver from AgNPs accumulates in various organs, with the highest concentrations in the intestine and stomach, raising concerns about systemic toxicity.

Argyria

Prolonged exposure to silver can lead to argyria, characterized by blue–gray skin staining.

Dose-dependent toxicity

AgNPs have toxic effects that vary with dosage; dosages over 20 mg/kg are harmful, whereas a limit of <18 mg/kg body weight is deemed safe.

Absorption mechanisms

AgNPs have complex absorption mechanisms, with oral administration leading to lower absorption rates and higher fecal excretion compared to smaller molecules, which can complicate the assessment of their toxicity.

Strategic approaches to overcome toxicity concerns for AgNPs

Employing green synthesis methods

Biogenic production of AgNPs utilizing plant extracts (especially polysaccharides) or microorganisms can produce more biocompatible and less toxic NPs compared to chemical synthesis [37].

Optimizing physicochemical properties

Modifying the physical property and surface chemistry of AgNPs can minimize toxicity while maintaining their desired antimicrobial effects.

Developing biocompatible coatings

Coating AgNPs with biocompatible materials such as polymers or biomolecules can reduce their toxicity and enhance their stability and targeting capabilities [39].

Conducting thorough toxicity assessments

Comprehensive studies (*in vitro* and *in vivo*) are required to examine the safety and biodistribution of AgNPs, considering factors such as dose, exposure route, and end-point measurement time [40].

Approaches of AgNPs/polymer functionalized AgNPs in dental applications

Preventive dentistry

Salas-López *et al*. assessed antibacterial activity of AgNP and "self-etching adhesive" activity, converted by comparing micro-leakage of AgNP-based sealants with normal sealants. The three folds reduced fluorescence activity of AgNPs group concluded that AgNPs-based sealant significantly suppressed tooth de-mineralization and enhanced re-mineralization in comparison to the conventional sealant [41].

Endodontics

Afkhami *et al*. in a study revealed that AgNPs outperformed 2.5% sodium hypochlorite in terms of their antibacterial and cytotoxic properties. Adding sodium hydroxide and ethanol allows AgNPs to penetrate deeper and access dentin canals and tubules. Thus, AgNPs successfully decreased the intracanal count of *Enterococcus faecalis* [42].

Dental implants

Implants are better than temporary prostheses or permanent bridges for replacing teeth. A study by Niska *et al*. demonstrated that carboxymethyl cellulose (CMC) and sodium alginate encapsulated AgNPs have antibacterial and biofilm prevention property. As a result, CMC-capped AgNPs inhibited a greater number of Gram-negative bacteria, aiming for improved action against oral anerobic bacteria. Thus, the efficacy of polymer-functionalized AgNPs in dental therapy was explored [43].

Anticancer treatment

The implication of AgNPs with berberine that could form an effective anticancer treatment combination where low doses of AgNPs inhibit the growth of a cancer cell line was discussed by Mallineni *et al*. Nanocarriers act on only cancer cells and not on normal cells, hence lowering the general side effects of chemotherapy and are advanced treatment methods [8]. The innovative strategies utilizing AgNPs and polymer-functionalized AgNPs are detailed in Table 2.

POLYSACCHARIDES IN DENTAL APPLICATIONS

Polysaccharides play a plethora of roles in antimicrobial activity, thereby being used in dental formulations as polymeric NPs to synthesize AgNPs for dental application and functionalize AgNPs. Natural polysaccharides, being biocompatible, are used to entrap a therapeutic modality to target specific areas, synergize with AgNP to heighten the antimicrobial property, and are flexible for functionalization. Besides these, polysaccharides also sustain the release of entrapped drugs or entrapped AgNP for controlled release, improving the stability of AgNPs. Fig. 5 reflects the antimicrobial activity of polysaccharides.

Impact of synthesis conditions on polysaccharide-stabilized AgNPs formulations

Synthesis of NPs significantly influences the physical characteristics and functional capacities of polysaccharide-stabilized AgNPs. By

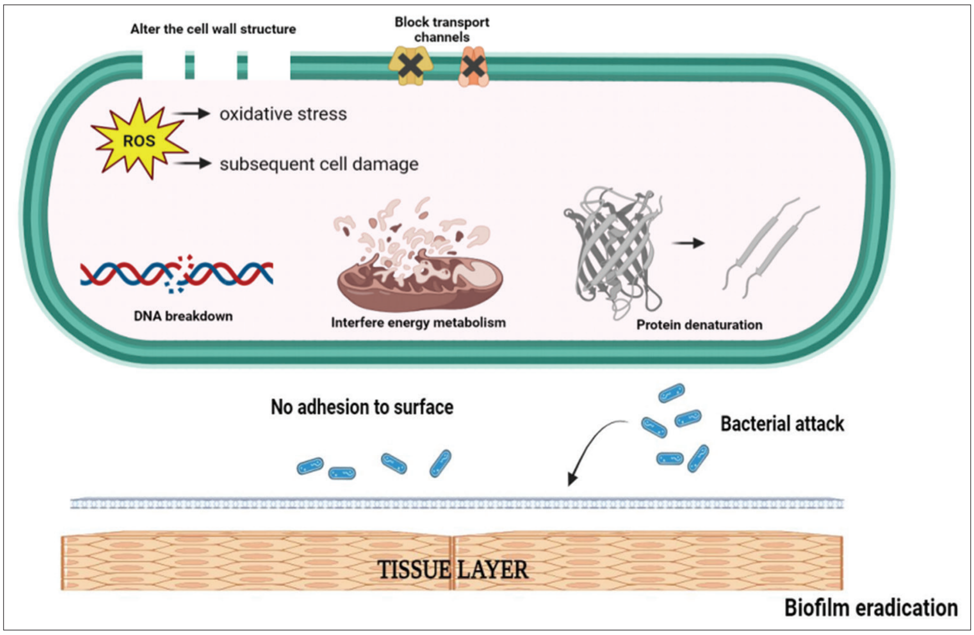

Fig. 5: Mechanism of antimicrobial activity of polysaccharides

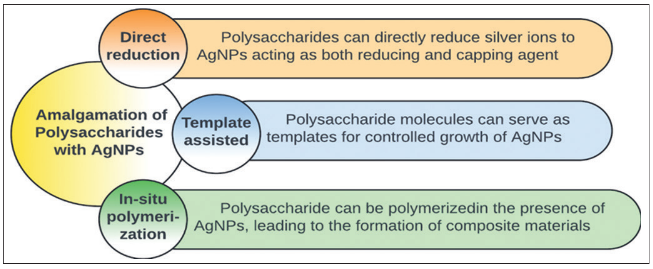

Fig. 6: Synthetic techniques for formulating polysaccharide functionalized silver nanoparticles

optimizing factors such as the type of polysaccharide, reaction parameters, and concentrations, researchers have tailored AgNPs for specific applications, enhancing their effectiveness in areas such as antimicrobial treatments and catalysis depicted by some case studies [55,56].

Yang *et al*. have found that the type of polysaccharide (e.g., exopolysaccharides from fungi) used in the production of AgNPs varies their size and antibacterial property. Apart from that the reaction parameters (reaction time, temperature, and pH) affect the particle size and stability of AgNPs (1–5 h at 100°C) leading to desired sizes [57]. Sharma *et al*. have studied the concentration of reactant (polysaccharide and silver nitrate) on the particle size and have observed that higher polysaccharide concentrations lead to stabilized AgNPs but with increased particle size [58]. Wang *et al*. have studied and explained the influence of catalytic properties on shapes and sizes of AgNPs formed during synthesis [56]. A study by Taher *et al*. explained the effect of synthesis techniques of AgNPs on their size and morphology and found the efficiency of reduction techniques to synthesize small uniformly dispersed AgNPs [44].

Amalgamation of polysaccharides with AgNPs

The amalgamation of polysaccharides in AgNP synthesis has drawn significant attention in recent years because polysaccharides have properties that enhance the stability, biocompatibility, and functionality of AgNPs. Various synthesis techniques are employed for this purpose, including direct reduction, template-assisted synthesis, and *in situ* polymerization are illustrated in Fig. 6 [59,60].

APPLICATIONS OF POLYSACCHARIDES IN AgNPs-BASED FORMULATIONS

Alleviating toxicity

Studies indicate that polysaccharides can lessen the toxicity of AgNPs to organisms. For instance, extracellular polymeric substances (EPS) can lead to a higher tolerance to AgNPs, as these substances can alter the toxic pathways associated with Ag^+ ions and AgNPs. Furthermore, biofilm formation can prevent bacterial attack, reducing cellular toxicities [61].

Stabilization

Polysaccharides, such as chitosan, CMC, and alginate, provide steric stabilization to AgNPs, preventing agglomeration and enhancing colloidal stability. The hydrophilic nature of these polysaccharides creates a protective coating for the NPs, essential for maintaining their size and preventing aggregation over time [62].

Functionalization

The functional groups present in polysaccharides can facilitate the attachment of bioactive molecules, enhancing the therapeutic potential of AgNPs. For instance, polysaccharides can be modified to include carboxyl or hydroxyl groups, which can interact with the surface of AgNPs, promoting better drug loading and release profiles in drug delivery applications [63,64].

Biocompatibility

Natural polysaccharides are generally biodegradable and biocompatible, making them well accepted in biomedical field. The use of polysaccharides in AgNP formulations can reduce cytotoxicity and improve the safety profile of the NPs, making them more acceptable for clinical use [62].

Enhanced antimicrobial activity

Combining AgNPs with polysaccharides has been shown to improve their antimicrobial properties. For instance, studies have demonstrated that AgNPs stabilized with polysaccharides exhibit enhanced antibacterial activity against most pathogens, as well as Gram-positive and Gram-negative bacteria. This synergistic effect is attributed to the combined action related to silver ions and the polysaccharide matrix [65]. Table 3 highlights the therapeutic effects of polysaccharide-functionalized AgNPs.

Table 2: Approaches of AgNPs/polymer functionalized AgNPs in dental applications

Sl. No.	NPs	Dosage form	Synthesis method	Microorganism	Parameters studied	Therapeutic effects	References
1.	Silver nanoparticles (AgNPs)	Solution	Green synthesized and then functionalized with chitosan and sodium fluoride.	*Streptococcus mutans*	Degree of mineralization=6.43, p<0.05*	Improved antibacterial properties and potential for remineralizing and strengthening demineralized dentine	Cifuentes-Jiménez *et al.* [4]
2.	Silver nanoparticles (AgNPs)	Powders	Green synthesis from extract leaves of Alocasia indica	*S. aureus*	99% of bacterial inhibition	Inhibition against *S. aureus* bacteria, indicating strong antibacterial properties	Hossain *et al.* [44]
3.	Silver nanoparticles	Acrylic resin (Lucitone 550)	Chemical Reduction Method	*Candida albicans*	Decreased enumeration of colony-forming units (CFUs); p<0.01*	Reduced biofilm growth without compromising the flexural strength of the acrylic resin	Takamiya *et al.* [45]
4.	Silver nanoparticles (AgNPs)	Dental composites	Chemical method	*S. aureus*, *P. aeruginosa*	0.025% inhibition for *P. aeruginosa* and a minimum of 0.1% inhibition for *S. aureus*; p<1*	Excellent antimicrobial activity promoting osseointegration	Alcudia *et al.* [46]
5.	Silver nanoparticles (AgNPs)	Nanoparticles	Bio-reduction process by mixing gum arabic extract	*Streptococcus mutans*	ZOI=18.30±0.5 nm; p<0.05*	Exhibit significant antibacterial action, inhibiting biofilm formation	Al-Ansari *et al.* [47]
6.	AgNPs immobilized Halloysite Nanotubes (HNTs)	Dental resin composite	Chemical method	*S. mutans*	ZOI=10.0±0.5 mm; p<0.05*	Improved mechanical properties and exhibit antibacterial activity	Barot *et al.* [48]
7.	Silver nanoparticles (AgNPs)	Toothpaste and mouth rinses	Green synthesis from the leaf extract of *Justicia glauca*	*S. mutans*	MIC value=50 μg/mL	Show promising antimicrobial, antifouling, and remineralizing effects	Ahmed *et al.* [1]
8.	Silver nanoparticles (AgNPs)	Dental adhesives, sealers	Chemical method	*Escherichia coli, Staphylococcus aureus*	Considering effects on Gram-positive along with Gram-negative bacteria	Significant antimicrobial potential, making them effective in dental infection prevention, prophylaxis, and disinfection.	Fernandez *et al.* [49]
9.	Silver nanoparticles (AgNPs)	Nanoparticles	Biological synthesis	*Streptococcus mutans*	ZOI=16.7±0.0 μg/mL; p<0.05*	Exhibit strong antibacterial effects and improve clinical outcomes	Espinosa-Cristóbal *et al.* [50]
10.	Silver oxide nanoparticles (Ag_2O NPs)	Powder	Green synthesis using prop root extract of *Ficus benghalensis*	*Streptococcus mutans*, *Lactobacilli* spp.	Maximum zone of inhibition at 15 mm against *S. mutans* and 18 mm against *Lactobacillus acidophilus* at 250 μg concentration; p<0.05*	Antibacterial activity suggests potential use in toothpaste as a germicidal agent.	Manikandan *et al.* [51]

(Contd...)

Table 2: ***(Continued)***

Sl. No.	NPs	Dosage form	Synthesis method	Microorganism	Parameters studied	Therapeutic effects	References
11.	Silver nanoparticles (AgNPs)	Glass ionomer cement	Green synthesis from *Mangifera indica* leaves	*Escherichia coli, Staphylococcus aureus*	ZOI found to be 1.2 mm *(E. coli)* and 1.5 mm (*S. aureus*) in conc. of 8 µg/mL	They exhibit promising antibacterial activity, making them practical for dental restoration and antibacterial applications.	Sundeep *et al*. [52]
12.	Dextran-stabilized silver nanoparticles	Nanoparticles	Chemical synthesis	*Staphylococcus aureus*	36 mm diameter of the inhibiting zones	Exhibit significant antibacterial properties	Bankura *et al*. [53]
13.	Silver nanoparticles (AgNPs)	Nanoparticle's solution	Green synthesis from leaf extract of *Maranta arundinacea* L.	*Salmonella* Typhi	ZOI=7.033±0.033 mm at 250 µL concentration; $p<0.05$*	Exhibit reasonable antimicrobial activity	Rokhade *et al*. [54]

*Significant difference. *S. mutans*: *Streptococcus mutans*, *E. coli: Escherichia coli, S. aureus: Staphylococcus aureus*, MIC: Minimum inhibitory concentration, ZOI: Zone of inhibition

Table 3: Polysaccharide-based AgNP system for dental treatments

Sl. No.	NPs type	Polysaccharide combined	Dosage form	Therapeutic effects	References
1.	TiO2 nanoparticles	Chitosan	Dental resins	Flexural strength improved by addition of 0.5%w/w Titanium dioxide, while 0.5%w/w chitosan increased compressive strength. Combining both enhanced self-healing efficiency and biocompatibility	Ravandi *et al*. [33]
2.	Silica-coated silver nanoparticles	CMC	Aqueous suspensions	Potent antimicrobial action against *Streptococcus mutans* and significant inhibition of biofilm formation	Rodrigues *et al*. [66]
3.	Silver nanoparticles	*Chlorella vulgaris* soluble polysaccharides	Nanoparticles	Minimize infections and avoid bacterial colonization on dental prostheses	El-Naggar *et al*. [60]
4.	Silver fabricated Iron oxide (Fe2O3) nanoparticles	Fucoidan, carrageenan	Gels, pastes	They exhibit antibacterial, antifungal, and anti-inflammatory properties, making them effective in preventing dental infections and promoting oral health.	Yosri *et al*. [67]
5.	Silver nanoparticles (AgNPs)	Alginate	Dental cap	The anti-inflammatory effects of AgNPs result in reducing inflammation and promoting tissue healing.	Perkasa *et al*. [68]
6.	Silver nanoparticles (AgNPs)	Chitosan	Hydrogel	Antimicrobial formulation and exhibits high antibiofilm activity.	Amasya *et al*. [69]
7.	Silver nanoparticles (AgNPs)	Chitosan	Nanocomposites	Inhibitory action against *S. aureus* and *C. Parapsilosis*	Oviya *et al*. [70]
8.	Titanium-coated silver nanoparticles	Chitosan	Dental implant	Antibacterial property against *S. mutans* and *P. Gingivalis*	Divakar *et al*. [71]
9.	Silver nanoparticles	Cellulose	Bone cements	Improve porosity and antibacterial properties	Wekwejt *et al*. [72]

CMC: Carboxymethyl cellulose

COMPARATIVE ANALYSIS OF FUNCTIONALIZED AgNPs

The antimicrobial activity of different polymer-conjugated AgNP systems and the effect of varying functionalization processes are crucial aspects in combating dental infections and biofilm formation in recent inventions. Zone of inhibition (ZOI) and minimum inhibitory concentration (MIC) are quantitative measurements of antimicrobial action. While the ZOI is a qualitative measure of inhibitory action, MIC values identify the minimum amount needed to suppress bacterial growth. A graph (Fig. 7) was plotted to analyze the variation in antimicrobial activity (ZOI) against *S. mutans*, among different nanoparticulate systems, highlighting their different dosage form in enhancing dental treatments. It shows that AgNPs are most effective against *S. mutans*, advocating its use as antimicrobial agent. Jimenez *et al.* in a study explained that chitosan and fluoride functionalized AgNPs were evaluated for potent dental application, causing remineralization and strengthening dentine. Therefore, further research of polymer functionalized AgNPs with respect to its antimicrobial study may show a higher antimicrobial potential due to the additive effect of antimicrobial potential of polymer and AgNPs.

Table 4: List of silver nanoparticle's patents granted

Patent no.	Patent title	Claim	Date of Patent grant	References
US 11,771,628 B2	"Methods of making silver nanoparticles and their applications"	The invention of microparticles coated with polysaccharide-coated silver nanoparticles. Also revealed are processes for producing silver nanoparticles and their applications in dental treatment	October 3, 2023	[73]
US 11,453,058 B2	"Preparation of highly stable concentrated dispersions of silver nanoparticles using synergistic dispersing agents"	Techniques for producing highly stable concentrated silver nanoparticle dispersions to minimize the ionic strength of the reaction medium and end silver dispersions.	September 27, 2022	[74]
US 2020/0171081 A1	"Method for producing Gum Arabic encapsulated metal nanoparticles"	The invention includes preparation of biocompatible metal nanoparticles stabilized using gum arabic material that can be delivered *in vivo* for carrying out therapy for human or animal subjects	June 4, 2020	[75]
EP3 057 617B1	"Nanoparticle containing hydrogels"	The invention relates to nanoparticle-containing hydrogels and their synthesis methods and also its usefulness as an antimicrobial and/or antibacterial agent	April 1, 2020	[76]
US 2018/0280431 A1	"Process for obtaining the product for prevention, interruption of dental caries lesions, and teeth remineralization and obtained product"	The invention designed metal particles and polysaccharides, aiming at preventing the development of tooth lesions caused by dental caries	Oct. 4, 2018	[77]
US 10,064,891 B2	"Assembly of micelle aggregates of surfactant micelles and silver nanoparticles and use as antibacterial agent"	A collection of aggregated micelles, consisting of nano-sized particles of metallic silver used in the treatment of bacterial infections.	September 4, 2018	[78]
US 8,927.024 B1	"Antimicrobial polyanhydride nanoparticles"	The invention provides compositions of polyanhydride microparticles or nanoparticles to treat microbial infections in animals	Jane 6, 2015	[79]
US 8,361,553 B2	"Methods and compositions for metal nanoparticle- treated surfaces"	The invention described here deals with the composition of metal nanoparticles, and the application of certain stabilizing agents offers flexibility in designing the properties of the nanoparticles for diverse uses	Jane 29, 2013	[80]

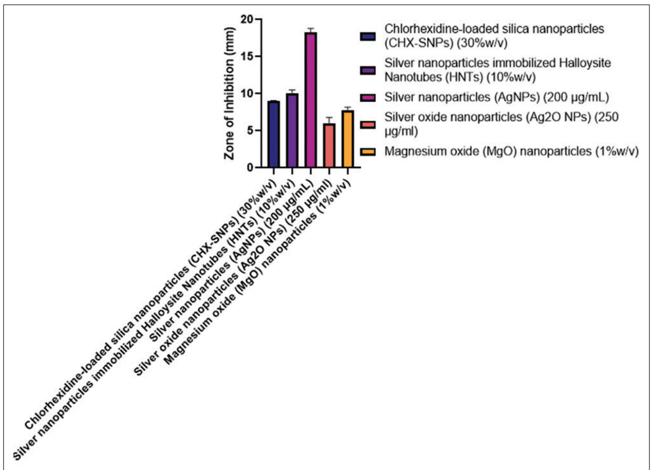

Fig. 7: Comparing nanoparticles system based on antimicrobial activity of *Streptococcus mutans*

Patents

AgNPs and their polymer functionalized systems are leading the way in introducing novel solutions in dental treatment, primarily based on their antimicrobial potential. The patents in Table 4 collectively reflect the innovation in employing such NPs systems in practical antimicrobial uses across various fields.

CONCLUSION

Polysaccharide-functionalized AgNPs are a paradigm shift in dental therapeutics that unite efficacious antimicrobial action with enhanced biocompatibility. This review delineates how polysaccharide matrices, through modulation of synthesis protocols, fine-tune AgNP stability, bioavailability, and targeted biofilm disruption, minimize risks of cytotoxicity from metal NPs. Comparative studies show that AgNP-conjugated systems surpass unmodified counterparts in *S. mutans* resulting in the elimination of biofilm and reduced enamel demineralization through prolonged ion release and augmented mucosal adhesion. However, clinical translation demands rigorous standardization of synthetic parameters to ensure batch-to-batch reproducibility and long-term safety. A novel synthesis-structure-activity relationship paradigm is proposed to minimize environmental footprint. Future innovation has to be aimed at dual-functional systems that integrate diagnostic function with on-demand antimicrobial activation, placing polysaccharide-AgNP hybrids as cornerstone technologies in precision dentistry. Therefore, the review emphasizes future research on functionalizing AgNPs with natural polysaccharides to impart an additive antimicrobial effect and emerge as a promising stable and potent dental formulation.

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AUTHORSHIP CONTRIBUTIONS

Prosun Ganguly: Conceptualization, Writing - original draft. Moumita Chowdhury: Review and editing. Aniket Hajra and Swarnakamal Bag: Data collection and analyzing literature.

CONFLICT OF INTEREST

The authors have no conflict of interest in this work.

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Nil.

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