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Silver Nanoparticles in Biomedical Applications: Synthesis, Biocompatibility, and Future Challenges

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Abstract : Silver nanoparticles (AgNPs) have attracted a lot of significant attention during the last few decades, due to their distinct physicochemical characteristics and wide range of biomedical uses. AgNPs are very hazardous to microorganisms but less toxic to humans. As a result, silver nanoparticles are well suited for use in biomedical, antibacterial, catalytic, human health, environmental remediation, etc. applications. AgNPs are widely employed in biomedical applications due to their antibacterial properties, bio-detection and labelling, bio-magnetic separations, drug transport, imaging, bone cement, therapies, etc. Silver nanoparticles are potential catalytic materials for a variety of applications due to their superior optical and electrical characteristics. As a result of their capacity to produce reactive oxygen species, localised hyperthermia, and deliver therapeutic payloads has led to investigations in targeted drug delivery systems, photothermal therapy, and photodynamic therapy.

The use of silver nanoparticles in environmental bioremediation is another possible use. The ability of AgNPs to effectively disinfect surfaces, water, air, and more makes them a valuable tool for environmental treatment. As a result, silver nanoparticles might be regarded as useful for having a variety of applications for the good of humans. The numerous biomedical uses of silver nanoparticles are summarized in this abstract, emphasizing their potential as adaptable tools for medication administration, therapy, and diagnostics.

Index Terms **- Silver nanoparticles, Biomedical application, Environmental bioremediation, Future challenges.**

1. INTRODUCTION

A remarkable advance has been made in healthcare and medical interventions as a result of the convergence of nanotechnology and biomedicine. Due to their distinctive physicochemical properties and multifaceted biomedical applications, silver nanoparticles (AgNPs) have emerged as an especially fascinating class of nanomaterials. A new era of precision medicine is dawning with the advancement of AgNPs, which possess unique attributes that make them promising candidates for applications in diagnostics, therapy, and drug delivery (Jain et al., 2009). AgNPs' unique characteristics are a result of their quantum effects and nanoscale size. Their high surface area-to-volume ratio and capacity for LSPR (localised surface plasmon resonance) endow them with a variety of properties that have drawn the interest of both researchers and medical professionals. AgNPs have subsequently attracted considerable attention and inquiry in the field of biomedicine (Liao, Li, & Tjong, 2019).

AgNPs have attracted a lot of attention as potent antibacterial and antimicrobial agents. With the rise of multidrug-resistant pathogens, the need for effective antimicrobial strategies has become paramount. With their capacity to damage bacterial cell walls and prevent the growth of biofilms, AgNPs offer an appealing treatment for infectious diseases. They are used in wound healing, medical device coatings, and cleaning procedures, demonstrating their ability to address important clinical challenges (M. Rai, Yadav, & Gade, 2009). Diagnostics is a further area where AgNPs have shown remarkable promise. Ultrasensitive biosensing platforms have been made possible by their distinctive plasmonic features, particularly surface-enhanced Raman scattering (SERS) and fluorescence enhancement. These platforms allow for the quick and precise detection of biomolecules including proteins and nucleic acids, which may have consequences for the early diagnosis, prognosis, and monitoring of diseases (Willets & Van Duyne, 2007).

AgNPs display a variety of mechanisms in the therapeutic realm that show potential for individualised treatment modalities. Interest in their use for cancer treatment has been sparked by their capacity to produce reactive oxygen species for photodynamic therapy, create localised hyperthermia through photothermal effects, and contain therapeutic payloads for targeted drug administration. AgNPs offer a wide range of possibilities, but their biocompatibility and safety continue to be major worries. This paper also addresses these challenges, explores potential cytotoxicity and outlines techniques to improve AgNPs' biocompatibility for secure clinical application (AshaRani, Low Kah Mun, Hande, & Valiyaveettil, 2009).

This study aims to investigate the various medicinal uses of AgNPs, highlighting their potential to transform patient care, therapy modalities, and diagnostics. AgNPs' distinctive qualities, such as their tunable optical characteristics, ease of functionalization, and biocompatibility with biological systems, are what give them their diverse range of uses. AgNPs have shown to be incredibly useful in a number of important fields by utilising these characteristics (Siavash Iravani, 2011). In the first section of this study, the methodologies of AgNP production and characterisation are covered along with the numerous strategies used to engineer and customise AgNPs for diverse biomedical applications. The following sections dig into the particular fields where AgNPs have had a big impact.

The biomedical applications of silver nanoparticles have great potential to change the face of modern medicine. AgNPs provide creative approaches for identifying and treating diseases, improving patient care, and promoting personalised medicine by harnessing their unique properties. However, in order to fully utilise them while mitigating potential risks, thorough investigation and comprehensive understanding are essential (X.-F. Zhang, Liu, Shen, & Gurunathan, 2016).

2. SYNTHESIS AND CHARACTERIZATION OF SILVER NANOPARTICLES

Understanding the structure-property correlations of silver nanoparticles (AgNPs) and adjusting their properties for particular biomedical applications depend critically on their synthesis and characterization. AgNPs are synthesised using a variety of techniques, including chemical, physical, and biological ones. Analysing their size, shape, morphology, and surface characteristics is essential for understanding their behaviour and potential interactions with biological systems (Dawadi et al., 2021; Naganthran et al., 2022).

2.1. Synthesis of Silver Nanoparticles

Silver nanoparticles can be synthesized by a variety of physical, chemical, and biological processes. These procedures each have some benefits and drawbacks. They are briefly described in **Table 1** (Mukherjee & Patra, 2017; Naganthran et al., 2022; Simões, Ottoni, & Antunes, 2020; Xu et al., 2020).

Table 1. Difference between three types of synthesis

Chemical method	Physical & Mechanical method	Biological method
High yield, high purity and reproducible	Produce bulk amount of NPs	Cost effective, eco-friendly, one step fast process
Time saving process	Produce uniform products	Does not require additional capping or stabilizing agent
Controllable route of synthesis	Does not require uses of chemical reagents	Highly stable NPs can be produced at room temperature
Less eco-friendly (cause pollution)	High cost	Cause imbalance ecology (over usage)
Toxic (chemical usage)	Toxic (radiation)	Weather dependant on active biomolecules production

Chemical reduction methods, like the Turkevich method, a reducing agent reduces silver ions in the presence of a stabilising agent. With the use of these techniques, reaction parameters can be precisely adjusted to control particle size and shape. Trisodium citrate serves as a stabilising and reducing agent in the Turkovich method while $AgNO_3$ serves as the silver precursor. The silver nanoparticles produced by this technique range in size from 30 to 60 nm on average (S. Iravani, Korbekandi, Mirmohammadi, & Zolfaghari, 2014). The size of the nanoparticle might vary depending on a number of parameters. The impact of the dispersion provided by polyvinylpyrrolidone (PVP) is the initial factor that alters the size of nanoparticles. When PVP is added a pintsized amount, it cannot coat the AgNP fully. During that time, a different particle moves in closer and forms a larger particle. However, if PVP is significantly higher, it also inhibits the particle from remaining smaller. It is best to synthesise with a specified quantity of PVP. Secondly, the particle size can be altered by the Amine also. In aqueous solution, amine reduces the silver ion, resulting in a larger particle. Lastly, High temperature nanoparticle synthesis frequently results in larger and non-spherical particles in colloidal solutions. It shows the opposite at low temperatures. (Alim-Al-Razy, Asik Bayazid, Rahman, Bosu, & Shamma, 2020; Natsuki, 2015).

Physical techniques decrease silver ions and produce nanoparticles through high-energy processes and physical pressures. These processes have benefits including producing highly pure nanoparticles without the need of chemical reduction agents. AgNPs are produced using high-energy techniques like laser ablation and sputtering. Using a powerful laser beam to vaporise a silver object in a liquid environment is known as laser ablation. A vapour of silver atoms is created by the laser-induced ablation, and this vapour later condenses and forms nanoparticles. The AgNPs' size and form can be precisely controlled by this method (Amendola & Meneghetti, 2009). A silver target is bombarded with high-energy ions in a vacuum chamber during the physical vapour deposition process known as sputtering. Silver atoms are ejected from the target as a result of this bombardment, and these atoms later deposit as AgNPs on a substrate. Excellent control over particle size and high levels of purity are provided by sputtering (Asanithi, Chaiyakun, & Limsuwan, 2012). Silver is evaporated using gas condensation techniques in a regulated gas environment. The quick cooling of the silver vapour causes AgNPs to condense and form. This method can create highly uniform nanoparticles with controlled sizes (Kruis, Fissan, & Rellinghaus, 2000; Lee & Jun, 2019). A silver target is ablated in a vacuum using the precision technique of pulsed laser deposition (PLD). AgNPs are created by depositing the ablated material onto a substrate. PLD is appropriate for thin film deposition and provides control over nanoparticle size and composition (Zakaria, Menazea, Mostafa, & Al-Ashkar, 2020).

Biological methods utilize plants, microorganisms, or enzymes to synthesize AgNPs. This environmentally benign method of synthesis can produce well-dispersed nanoparticles with potential biomedical applications. Microorganisms including bacteria, fungus, and yeast are used in microbial synthesis as reducing agents to turn silver ions into AgNPs. Enzymes and biomolecules found in these microorganisms can efficiently reduce and stabilise the nanoparticles. The size and shape of the nanoparticles may be precisely controlled using this technology, which is also cost-effective (Narayanan & Sakthivel, 2010; Vijayaraghavan & Nalini, 2010). In plant-mediated synthesis, plant extracts or parts (leaves, stems, and roots) are used as reducing and stabilising agents for AgNPs synthesis. Plant extracts contain phytochemicals like flavonoids and polyphenols that play a crucial role in the reduction process. This method has the potential for large-scale production and is environmentally benign (Siavash Iravani, 2011; Singh, Kim, Zhang, & Yang, 2016). The reduction of silver ions to AgNPs during enzyme-catalyzed synthesis depends on the catalytic activity of enzymes. This approach frequently makes use of enzymes like laccase, glucose oxidase, and lysozyme. Enzymatic synthesis offers high specificity and control over nanoparticle characteristics (Singh et al., 2016). There is evidence that several macroalgae and microalgae species can biosynthesize AgNPs. Biomolecules found in these algae help reduce silver ions and stabilise the resulting nanoparticles. Algae-based synthesis is environmentally benign and offers potential for various applications (Mohandass et al., 2013). AgNPs with a biocompatible surface are often synthesised using biological methods, making them appropriate for use in biomedical applications. These nanoparticles have the potential to be used in drug delivery and therapies and exhibit minimal cytotoxicity (Castro-Longoria, Vilchis-Nestor, & Avalos-Borja, 2011).

2.2. Characterization Techniques

Characterization techniques, such as TEM, SEM, XRD, and UV-Vis spectroscopy, provide essential understanding of the size, shape, and plasmonic characteristics of AgNPs. A thorough comprehension of these aspects opens the door to the logical design of AgNPs with improved functionality for numerous biomedical applications. Transmission Electron Microscopy (TEM) is a powerful characterization technique widely employed in the fields of nanotechnology and materials research. It allows for high-resolution imaging and detailed analysis of the surface and internal structures of nanoparticles, including silver nanoparticles (AgNPs). TEM operates on the principle of transmitting a beam of electrons through a thin sample (typically less than 100 nanometers thick), which interacts with the sample to produce high-resolution images. The sample is exposed to an electron beam, some of which are scattered, refracted, or absorbed by the sample, while others pass through and are detected by a detector placed on the opposite side of the sample. TEM provides details on the distribution, size, and shape, and allowing precise and accurate tailoring of AgNPs for certain biomedical applications (Kim et al., 2007; M. Rai et al., 2009; Xie, Ye, & Liu, 2006).

A potent imaging method for characterising nanomaterials, such as silver nanoparticles (AgNPs), is scanning electron microscopy (SEM). At a nanoscale resolution, SEM offers thorough topographical and morphological details about the surface of materials. SEM can be used to determine the nanoparticles' shape (e.g., spherical, rod-shaped) and surface characteristics (e.g., roughness, porosity) (Abou El-Nour, Eftaiha, Al-Warthan, & Ammar, 2010). SEM excels in surface imaging and three-dimensional visualisation but does not provide the same level of internal structural information as Transmission Electron Microscopy (TEM). By analyzing the images and making accurate measurements of each AgNP or aggregate, SEM enables the assessment of nanoparticle size. For a variety of applications, including catalysis and drug delivery, SEM can visualize the distribution of AgNPs within a sample and determine whether they have a propensity to aggregate. AgNPs' surface alterations, coatings, or functionalizations, which affect how they interact with biological systems or other materials, can be examined using SEM (Misirli, Sridharan, & Abrantes, 2021; Shankar, Rai, Ahmad, & Sastry, 2004).

AgNPs can be structurally characterized using X-ray diffraction (XRD). The crystalline structure, crystal size, lattice parameters, and phase composition of nanomaterials can all be learned through XRD. This information is crucial for understanding the physical and chemical properties of AgNPs. XRD uses an X-ray source that emits X-rays of a specific wavelength. The periodic arrangement of atoms causes scattering when X-rays interact with the crystal lattice of AgNPs. Diffraction patterns result from this scattering, which are are collected and analyzed. AgNPs' crystal structure can be determined by analyzing the angles and intensities of diffracted X-rays (Bar et al., 2009; Shankar et al., 2004).

UV-Visible Spectroscopy is also a widely used analytical technique for characterizing silver nanoparticles (AgNPs). AgNPs' optical characteristics, such as their absorbance and surface plasmon resonance (SPR), which are important determinants of nanoparticle size, shape, and aggregation state, are revealed by this spectroscopy. AgNPs absorb particular wavelengths of UV-Visible light when it passes through the sample because of their size, shape, and aggregation state. Information regarding the optical characteristics of AgNPs can be gleaned from the position and intensity of absorption peaks. Using this spectroscopy the concentration of AgNPs in a solution can also be estimated by correlating the absorbance at a specific wavelength with the nanoparticle concentration (Hemmati et al., 2019).

3. BIOMEDICAL APPLICATIONS

AgNPs and their nanocomposites have created remarkable potential and notable applications in a variety of nanotechnology fields, particularly in biomedical therapeutics (or biomedical and therapeutic research), MRI (magnetic resonance imaging) contrast agents, drug delivery, and biomedical devices for the detection of numerous alarming diseases or complications (Abass Sofi, Sunitha, Ashaq Sofi, Khadheer Pasha, & Choi, 2022; Naganthran et al., 2022; Sharma & Bhargava, 2013). Furthermore, as AgNPs have evolved into a cutting-edge product of consumer appeal, their many biological and other uses are noteworthy. AgNPs are becoming more and more prevalent in many industrial domains, including food, textiles, healthcare, cosmetics, feminine/female hygiene, water purification, and pollution control in the environment. Additionally, thermal, electronics, engineering, energy, and magnetic field applications are where AgNPs are most frequently utilized (Akter et al., 2018). AgNPs are also promising for use in biosensing applications because the concentration of adsorbed molecules can regulate the wavelength of SPR (surface plasmon resonance) and because the SPR of AgNPs is substantially influenced by the surface-adsorbed molecules (Csáki, Stranik, & Fritzsche, 2018). Nanomaterials are utilized in many biomedical applications (Fig. 1), such as orthopedics/implants, thermal spray coatings, biodetection and labelling, biomagnetic separations, drug delivery, MRI contrast agents, and antimicrobials (Naganthran et al., 2022; Sharma & Bhargava, 2013).

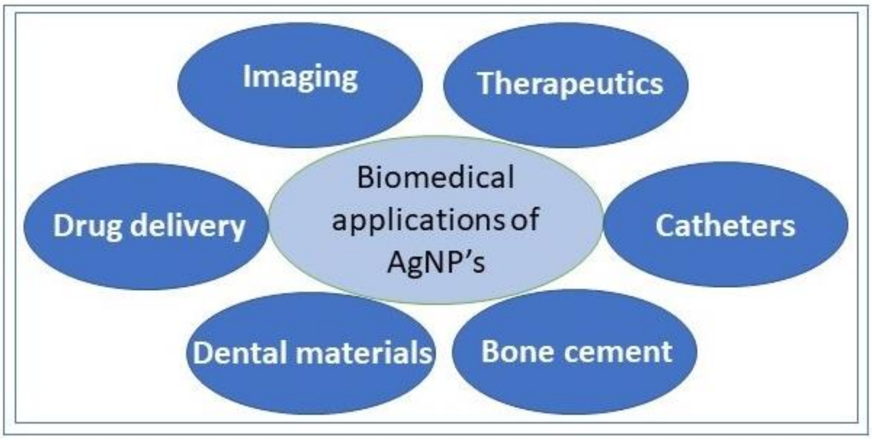

Fig. 1. Biomedical applications

3.1. Imaging

The usage of nanoparticles in imaging applications has grown during the previous 20 years (Choi & Sun, 2011). Silver nanoparticles have made new approaches in sensing and imaging applications possible with their wide range of detection modes, which include colorimetric, scattering, SERS (Surface Enhanced Raman Spectroscopy), and MEF (Metal Enhanced Fluorescence) techniques available at extremely low detection limits (Caro, M., Klippstein, Pozo, & P., 2010). Metal nanoparticles scatter light by combining absorption and scattering in their extinction spectra (K. Lance Kelly, Coronado, Zhao, & Schatz, 2003; K.L. Kelly, Jensen, Lazarides, & Schat, 2002).

Silver nanoparticles (AgNPs) have attracted a lot of interest for use in biomedical imaging applications due to their distinctive optical characteristics, biocompatibility, and potential to improve imaging modalities. AgNPs are perfect for imaging applications because of their surface plasmon resonance (SPR) effect, which produces a high absorption and scattering of light. AgNPs have been applied to a number of optical imaging methods, including multiphoton imaging and surface-enhanced Raman scattering (SERS). SERS enhances Raman signals from molecules close to AgNPs' surface by taking advantage of their SPR effect, making molecular detection and imaging more sensitive. AgNPs combined with multiphoton imaging increase signal intensity, allowing for more contrasted deep tissue imaging (Tian, Ren, & Wu, 2002).

AgNPs can also be utilized as contrast agents in photoacoustic imaging, a technique that produces high-resolution images by generating acoustic signals from significant light absorption. This method makes it possible to visualize the blood vessels and deep tissues (Jokerst & Gambhir, 2011). AgNPs' high atomic number allows them to improve contrast in X-ray imaging. AgNPs can boost the sensitivity of X-ray imaging and make soft tissues more visible when added to contrast agents (Mondal, Raj, Roy, & Poddar, 2018). AgNPs coated with magnetic materials have the potential to function as dual-modal contrast agents in both optical and MRI imaging (Mishra & Kannan, 2017; Yamini et al., 2022). Additionally, AgNPs can be functionalized with fluorescent molecules to provide focused imaging and diagnosis. Their enhanced fluorescence signals result in increased sensitivity due to their plasmonic characteristics (Gahlaut, Pathak, & Gupta, 2022; Goldys & Drozdowicz-Tomsi, 2011).

3.2. Silver nanoparticles in therapeutics

Silver nanoparticles (AgNPs) have gained significant attention in the field of biomedical therapeutics because of their unique physicochemical properties and potential applications (Burduşel et al., 2018a). These nanoparticles have potential prospects for a range of therapeutic applications because of their antibacterial, anti-inflammatory, and wound-healing qualities (Kaushal et al., 2023). The process of healing a wound is intricate and multi-step, requiring the integration of activities of numerous tissues and cell lineages (Martin, 1997). Here, we will explore the therapeutic uses of silver nanoparticles in the biomedical applications with pertinent references supporting their use.

Strong antibacterial activity of silver nanoparticles is demonstrated against several pathogens, such as bacteria, viruses, and fungus (Bruna, Maldonado-Bravo, Jara, & Caro, 2021; M. K. Rai, Deshmukh, Ingle, & Gade, 2012). Silver nanoparticles are extremely potent fungicide as well as having antiviral properties (Galdiero et al., 2011). They have the ability to damage microbial cell membranes, obstruct cellular functions, and stop pathogen growth and multiplication (More et al., 2023). Because of this characteristic, AgNPs are now included in medical device coatings, wound dressings, and even the treatment of infections that are resistant to conventional antibiotics (Pal, Tak, & Song, 2007; M. K. Rai et al., 2012; M. Rai et al., 2009). By promoting cell proliferation, migration, and tissue regeneration, silver nanoparticles aid in the healing of wounds (Dakal, Kumar, Majumdar, & Yadav, 2016). The dressing containing silver nanoparticles helps the wound site by avoiding bacterial contamination (Sibbald et al., 2007). Moreover, they have the ability to control inflammation, lessen the development of scars, and increase collagen deposition, which promotes quicker and more efficient wound healing (Franci et al., 2015; Sharmin et al., 2021).

Silver nanoparticles have demonstrated promises in the treatment of cancer therapy due to their capacity to specifically target cancer cells while sparing healthy cells (Huy, Huyen, Le, & Tonezzer, 2020). They can be functionalized with anticancer drugs or targeting ligands to improve treatment efficacy and enable site-specific drug delivery (Chehelgerdi et al., 2023; Gavas, Quazi, & Karpiński, 2021; Gomes, Martins, & Prior, 2021; Montalvo-Quiros et al., 2019).

The silver nanoparticles have a wide range of biomedical applications in therapeutics, like antimicrobials, wound healers, and cancer treatment instruments. But, it is crucial to remember that additional study is required to completely comprehend their safety profiles and maximize their use in a range of medicinal applications.

3.3. Silver impregnated catheters

Due to their unique antimicrobial properties AgNPs have gained significant attention in the field of biomedical applications. One of the prominent applications is in the development of silver-impregnated catheters, which are medical tools that make it easier to administer or drain fluids in a variety of clinical contexts. Silver nanoparticles are coated or impregnated into these catheters to inhibit microbial colonization and lower the risk of catheter-associated infections (CAIs), which can cause patients to experience life-threatening consequences (Goda et al., 2022; Werneburg, 2022).

Catheter-associated infections are a serious concern in healthcare settings as they can result in bloodstream infections and other consequences, especially for patients who are severely ill or immunocompromised. One of the main causes of these infections is the colonization of biofilm-forming bacteria at the catheter sites. Catheters infused with silver have been developed as a way to lessen this problem (Darouiche, 2004; Rahuman et al., 2021; Trautner & Darouiche, 2004). A fresh range of silver-impregnated catheters is now available for use in therapeutic environments. Silver ions are bonded to inert ceramic zeolite in these catheters. Silverline (Spiegelberg GmbH and Co. KG, Hamburg, Germany) and ON-Q Silver Soaker^{TM} (I-Flow Corporation, CA, USA) are two well-known medical catheters coated with silver nanoparticles to prevent catheter-associated infections available commercially in the market (Chaloupka, Malam, & Seifalian, 2010).

Silver-impregnated catheters have a layer of AgNPs applied to their surface or the nanoparticles are mixed into the catheter's substances at the time of manufacture. This results in a steady discharge of silver ions from the catheter surface, fostering an environment that inhibits the growth of microorganisms and prevents the formation of biofilms (Lebeaux, Ghigo, & Beloin, 2014; Trautner & Darouiche, 2004).

3.4. Bone cement

One developing area that may have an impact on enhancing the functionality and performance of orthopedic implants is the biomedical use of silver nanoparticles (AgNPs) in bone cement. In orthopedic surgery, bone cement is frequently utilized to bind prosthetic implants to bone tissue, especially in joint replacement surgeries. AgNPs have drawn interest for their potential to improve the characteristics of bone cement and offer other advantages because of their distinct physicochemical qualities (Shi, Neoh, Kang, & Wang, 2006).

AgNPs' potent antibacterial qualities are a major reason why they are used to bone cement. AgNPs are proven to have strong antibacterial action against a variety of bacteria, including ones that are resistant to antibiotics. AgNPs can be incorporated into bone cement to assist reduce the possibility of post-operative infections, which can be a major issue during orthopedic surgeries (Wekwejt et al., 2019). The growth of *Staphylococcus epidermidis*, methicillin-resistant *S. epidermidis*, and methicillin-resistant *S. Aureus* was completely suppressed by poly (methyl methacrylate) bone cement treated with 1% silver nanoparticles (Alt et al., 2004; Arora, 2013; Lewis, 2022). Hence, employing silver nanoparticles as bone cement is an excellent alternative to using antibiotics is a great idea in orthopedic applications.

AgNPs have demonstrated promise in augmenting implant biocompatibility and stimulating bone healing (Burdușel et al., 2018a). Research suggests that AgNPs can improve the mineralization of bone tissue and stimulate osteoblast (bone-forming cell) (R. Zhang et al., 2015). This characteristic might be used to enhance how well orthopedic implants integrate with the surrounding bone tissue. AgNPs have the potential to enhance the mechanical characteristics of bone cement (Shi et al., 2006). AgNPs have been demonstrated to improve the cement matrix's overall strength and toughness, boosting its capacity to support loads and lowering the risk of implant failure (Huiling Liu et al., 2023; Świeczko-Żurek, Zieliński, Bociąga, Rosińska, & Gajowiec, 2022).

Silver ions can likewise be progressively released over time by designing AgNPs. Over an extended length of time, this regulated release method can offer continuous antibacterial activity, aiding in the prevention of infections. The release rate must be balanced to guarantee that antimicrobial action is efficient without having a harmful effect on healthy cells (Bruna et al., 2021; Prasher, Singh, & Mudila, 2018; Yin et al., 2020). While AgNPs offer promising benefits, but there are also worries regarding possible toxicity and long-term impacts on surrounding tissues when using them. A major issue in this area is balancing the concentration of AgNPs to produce the intended results without sacrificing biocompatibility (Hsin et al., 2008).

AgNPs in bone cement have a lot of potential for use in biomedicine to enhance the functioning and performance of orthopedic implants. AgNPs can contribute to better patient outcomes in surgical orthopedics by imparting antimicrobial characteristics, increasing bone regeneration, and potentially reinforcing mechanical strength. However, thorough research is necessary to deal with safety concerns and optimize the formulation of AgNP-enhanced bone cement for realistic clinical applications.

3.5. Dental materials

One intriguing approach to enhancing the characteristics and capabilities of different dental products is the incorporation of silver nanoparticles (AgNPs) into dental materials. AgNPs are appealing for biomedical uses in dentistry because of their distinctive qualities. Their huge surface area-to-volume ratio and tiny size make them especially useful in dental materials and other biomedical applications (Ayodeji Precious-Ayanwale, Donohué-Cornejo, CuevasGonzález, Espinosa-Cristóbal, & Simón Yobanny Reyes-López, 2018; Mobarak et al., 2023). AgNPs have been explored for their antibacterial, therapeutic, and tissue-regenerating characteristics in relation to dental materials. The addition of AgNPs to dental materials can improve oral health outcomes by inhibiting bacterial infections, biofilm development, encouraging tissue healing, and improving the functionality of dental restorative materials. Incorporating AgNPs into dental materials like composites, resin-based restorations, and dental adhesives can help inhibit bacterial growth and reduce the risk of dental caries and periodontal diseases (Corrêa et al., 2015).

The antibacterial characteristics of silver have long been recognized, and AgNPs have heightened antimicrobial activity because of their large surface area-to-volume ratio, which facilitates more interaction with the cell membranes of bacteria. AgNPs have strong antibacterial action against a variety of microorganisms, such as viruses, fungi, and bacteria. Strong antibacterial action of AgNPs has been demonstrated against oral pathogens that cause dental infections, such as *Streptococcus mutans*, *Porphyromonas gingivalis*, etc. (Beyth, Yudovin-Farber, Bahir, Domb, & Weiss, 2006). AgNPs have the ability to release silver ions continuously, guaranteeing prolonged antibacterial activity. This controlled release mechanism makes them suitable for dental materials like orthodontic appliances or dental implants that need to hold their antibacterial qualities over time (Dakal et al., 2016; Song & Ge, 2019).

Silver nanoparticles (AgNPs) can be added to toothpaste formulations, resin-based materials, and dental composites to provide a continuous release of silver ions that efficiently prevent the growth of microorganisms and the formation of biofilms on dental surfaces (Almatroudi, 2020; Siddiqi, Husen, & Rao, 2018; Some et al., 2018). AgNPs have the ability to prevent biofilms from growing on tooth surfaces. Biofilms are often associated with dental plaque and can lead to oral health problems. AgNP-enhanced dental materials can help improve oral hygiene and lower the risk of infections by preventing the formation of biofilms (Gallo et al., 2016; Hosnedlova et al., 2022; Khatoon, McTiernan, Suuronen, Mah, & Alarcon, 2018; Tran et al., 2020). Dental biofilms are intricate bacterial colonies that stick to dental restorations and tooth surfaces, causing plaque to form and other problems with oral health. It has been shown that AgNPs prevent the formation of biofilms and prevent bacteria from adhering to the dental surfaces. This characteristic is particularly helpful in avoiding biofilm-related issues with dental implants and other prosthetic devices (Allaker, 2013; Corrêa et al., 2015; Siddique et al., 2020). AgNPs are antimicrobial agents that can be used to treat periodontal disease and reduce inflammation and bacterial load. AgNPs can be incorporated into mouthwashes, periodontal gels, and other products to improve their therapeutic effects (Jiménez-Ramírez et al., 2021; Mallineni et al., 2023).

The strength of the binding between restorative materials and tooth surfaces can be increased by adding AgNPs to dental adhesives and bonding agents. This can result in more durable restorations and lower chance of developing secondary caries (Fatemeh, Mohammad Javad, & Samaneh, 2017; Jowkar, Shafiei, Asadmanesh, & Koohpeima, 2019). AgNPs can also be added to dental restorative materials like glass ionomer cements and resin composites. These materials not only gain the antimicrobial properties of AgNPs but also experience enhanced mechanical and physical characteristics due to the reinforcement provided by the nanoparticles. This enhancement in strength and durability is especially crucial for dental restorations subjected to chewing forces and oral environment challenges (Beyth et al., 2006; Corrêa et al., 2015; Fernandez et al., 2021; Mallineni et al., 2023). When added to a composite resin at varying concentrations, AgNPs show good mechanical properties and significant antimicrobial properties (Abed et al., 2022; Lei Cheng et al., 2012). A resin composite containing silver ion-implanted filler exhibit a good antimicrobial activity on oral *Streptococci* (Magalhães et al., 2012; Yamamoto et al., 1996). AgNPs have also been used in orthodontics, where they can be added to materials such as elastomeric ligatures and orthodontic adhesives. The antibacterial properties of AgNPs can be advantageous to these materials, lowering the possibility of plaque accumulation and associated complications during orthodontic treatment (Azarsina, Kasraei, Yousefi-Mashouf, Dehghani, & Shirinzad, 2013; Ferrando-Magraner et al., 2020; Mirhashemi et al., 2021).

AgNPs have also shown promise in accelerating wound healing and tissue regeneration. AgNPs can be added to materials used in periodontal therapy or root canal fillings to aid in the regeneration of injured tissues and hasten the healing process (L. Cheng et al., 2012, 2017). AgNPs have been studied in endodontics for their ability to fight germs in root canals. Root canal infections are often challenging to treat due to the intricate anatomy of the root canal system. Treatment outcomes can be enhanced by the use of AgNPs in endodontic sealers and medicaments, which can help eradicate bacteria and prevent re-infection (Afkhami, Forghan, Gutmann, & Kishen, 2023; Kasraei et al., 2014; Oncu et al., 2021).

Even though AgNPs have a lot of advantages, more research is needed to fully understand their biocompatibility and potential for cytotoxicity on oral tissues. It is essential to strike a balance between the beneficial effects and potential safety concerns associated with AgNPs. Rigorous research is needed to ensure that adding AgNPs to dental materials won't be harm the health of surrounding tissues (Burdușel et al., 2018b; Corrêa et al., 2015; Mallineni et al., 2023).

3.6. Drug delivery

The unique features of silver nanoparticles (AgNPs) in drug delivery have attracted a lot of attention in the biomedical field because they can improve drug stability, maximize therapeutic outcomes, and reduce adverse effects. AgNPs are a class of nanomaterials that come in sizes between 1 and one 100 nanometers, which provides them with distinct physicochemical features and a high surface area-to-volume ratio. This enables AgNPs to be functionalized with a variety of drug compounds, targeting ligands, and biomolecules for effective drug delivery (Gomes et al., 2021; Ivanova et al., 2019). Local drug targeting has several disadvantages because it increases drug concentrations in the area. For this reason, some improved drug delivery techniques are required. Certain particles in nanoparticles act as tools to make these tactics possible. Because of their minuscule size, which enables them to bind and stabilize proteins, penetrate cell membranes, and release lysosomes following endocytosis (Benyettou et al., 2015; De Jong, 2008).

Silver nanoparticles can serve as carriers for various therapeutic agents, including drugs, genes, and proteins. Their distinct surface characteristics facilitate the effective loading and regulated release of these payloads, improving the delivery of drugs to the intended tissues and minimizing systemic side effects (Gomes et al., 2021; Ivanova et al., 2019; Jain et al., 2009; Yusuf, Almotairy, Henidi, Alshehri, & Aldughaim, 2023). Targeted drug delivery to specific cells or tissues is made possible by functionalizing AgNPs with particular ligands, such as peptides or antibodies. Drug accumulation at the desired site can be improved by using this active targeting strategy, reducing off-target effects and increasing therapeutic outcomes (Seidu et al., 2022; Yusuf et al., 2023). AgNPs can encapsulate hydrophobic drugs to improved their solubility in aqueous environments. This can improve the delivery of drugs via a variety of methods, such as oral and intravenous administration. AgNPs can also protect sensitive drug molecules from oxidation and degradation, enhancing their stability during transportation and storage (Ahamed, AlSalhi, & Siddiqui, 2010; Gomes et al., 2021; Patra et al., 2018; Yusuf et al., 2023).

AgNPs can facilitate combination therapy by acting as carriers for multiple drugs or therapeutic agents. With the ability to target many pathways at once, this technique is very beneficial for treating complicated disorders like cancer. It increases treatment efficacy and decreases the emergence of drug resistance (Kovács, Igaz, Gopisetty, & Kiricsi, 2022; Yao et al., 2020). AgNPs exhibit strong absorption of near-infrared (NIR) light, which can be harnessed for photothermal therapy. AgNPs produce heat in response to NIR light, which can cause localized hyperthermia and the selective death of cancer cells while protecting healthy tissue. This combination of therapy and imaging, known as theranostics, shows promising potential in drug delivery (Hossain, Nanda, Selvan, & Yi, 2022; Hao Liu et al., 2023; S. Liu, Phillips, Northrup, & Levi, 2023). Additionally, AgNPs can be used as contrast agents for magnetic resonance imaging (MRI), optical imaging, and computed tomography (CT). They are appropriate for enhancing the sensitivity and precision of diagnostic imaging due to their potent light-scattering capabilities and tunable optical characteristics (Blasiak, Van Veggel, & Tomanek, 2013; Busquets, Estelrich, & Sánchez-Martín, 2015; Hsu et al., 2018; Khursheed et al., 2022).

4. BIOCOMPATIBILITY AND SAFETY CONSIDERATIONS

Understanding the biocompatibility and potential safety issues with silver nanoparticles (AgNPs) is crucial as these materials become more prevalent in biomedical applications. Despite the enormous potential of AgNPs, thorough evaluation of their interactions with biological systems, possible cytotoxicity, and long-term consequences is required to assure their safe clinical application (AshaRani et al., 2009).

AgNPs influence the biological responses of biological systems by interacting with them at the cellular and molecular levels. AgNPs have the ability to infiltrate cells, impacting cellular functions and potentially triggering inflammatory responses. Modifications to the surface, including functionalization with biomolecules, can modulate their interactions and biocompatibility. AgNPs' biocompatibility can be improved by surface modifications and coatings that decreases their cytotoxic effects. Engineering of the nanoparticle's surface charge, ligand functionalization, and polymer coatings can mitigate interactions with cells and reduce adverse effects (Huang et al., 2005). In vivo studies are crucial for evaluating the biocompatibility of AgNPs within complex biological environments. Long-term investigations can reveal AgNPs' possible accumulation, distribution, and persistence, providing information on their safety profiles over protracted time frames (Ivask et al., 2014).

AgNPs' cytotoxicity is strongly influenced by their size, shape, concentration, and surface chemistry. AgNPs have the ability to damage DNA (deoxyribonucleic acid), cause oxidative stress, and disrupt cellular membranes. AgNPs' biological activities are complicated by the release of silver ions, necessitating careful research into any potential adverse outcomes (AshaRani et al., 2009). To ensure patient safety, the use of AgNPs in biological applications requires adherence to regulatory standards. Before approving the clinical use of AgNPs, regulatory agencies require comprehensive toxicity assessments and risk evaluations.

5. FUTURE DIRECTIONS AND CHALLENGES

Silver nanoparticles (AgNPs) are being used increasingly in biomedical applications, providing a glimpse of the critical roles that these nanomaterials will play in diagnostics, therapy, and personalized medicine in the future. However, despite the promising potential, there are still issues to resolve and avenues to research in order to optimize the advantages of AgNPs in healthcare (X.-F. Zhang et al., 2016).

AgNPs have great potential for personalized medicine, which allows for patient-specific treatment plans. AgNPs can be functionalized with certain ligands, like antibodies or peptides, to enable targeted delivery to particular cells or tissues. This strategy reduces off-target effects and increases therapeutic effectiveness (Gomes et al., 2021; Ivanova et al., 2019; Xu et al., 2020). Combining AgNPs with various therapeutic modalities has shown the potential for synergistic effects. It may be possible to improve treatment outcomes by combining them with well-established medicines like chemotherapy or immunotherapy (Malindi, Barth, & Abrahamse, 2022; Mundekkad & Cho, 2022). Understanding the pharmacokinetics and in vivo biodistribution of AgNP-based treatments is essential for ensuring their safety and efficacy. AgNPs' behaviour over time can be better understood through long-term studies that clarify how they are metabolized, eliminated, and accumulate in the body (Burdușel et al., 2018a; Ferdous & Nemmar, 2020).

The multifunctionality of AgNPs can be enhanced by combining multiple functionalities into a single platform. This method reduces complexity and improves patient convenience by combining monitoring, therapy, and diagnostics into a single nanoparticle (Gurunathan, Kang, Qasim, & Kim, 2018; Yetisgin, Cetinel, Zuvin, Kosar, & Kutlu, 2020). AgNPs are moving closer to clinical uses, but there are ethical and societal considerations to take into account. Addressing issues and promoting public trust in the technology requires open research, ethical dissemination of findings, and participation of the public (Calderón-Jiménez et al., 2017). Regulatory approval is now a crucial factor as AgNPs get closer to clinical applications. Obtaining regulatory approval from health authorities, guaranteeing patient safety, and fostering confidence in the medical community all depend on thorough toxicity research, risk assessments, and standardized protocols. Realizing the revolutionary influence of AgNPs in contemporary medicine will depend on how these issues are handled while taking ethical and societal considerations into account.

6. CONCLUSION

Silver nanoparticles (AgNPs), with the potential to transform contemporary healthcare and improve patient outcomes, have gained significant attention in biomedical research due to their exceptional characteristics and multipurpose uses. While recognizing the difficulties and crucial factors that come with integrating AgNPs into clinical practice, this study has examined the broad and ever-changing field of AgNP applications in therapy, personalized medicine, and diagnostics.

AgNPs are a revolutionary class of tools in healthcare, providing novel approaches to everything from targeted medicines to diagnostics. AgNPs have facilitated ultrasensitive biosensing platforms and accelerated early disease detection and prognosis due to their distinct plasmonic characteristics and functional adaptability. Moreover, their incorporation into therapeutic modalities like drug delivery, photodynamic therapy, and photothermal therapy shows their potential to enhance conventional therapies and reinvent treatment modalities.

AgNPs in biomedicine have a lot of intriguing potential ahead of them. With the functionalization of AgNPs for targeted therapeutics, personalized medicine has the potential to transform treatment modalities by reducing side effects and improving therapeutic outcomes. Enhancing patient care and quality of life can be achieved through investigating synergistic medicines, developing multifunctional platforms, and gaining a thorough grasp of pharmacokinetics.

Notwithstanding the encouraging prospects, overcoming obstacles is still a crucial part of AgNPs' entry into the medical field. Thorough investigation is essential to decipher the complex relationships that AgNPs have with biological systems, guaranteeing safety, biocompatibility, and reducing potential side effects. Achieving approval and establishing trust in the healthcare community requires careful attention to regulatory factors, such as toxicity assessments and risk evaluations.

Finally, the multidisciplinary connection between nanotechnology and biomedicine is demonstrated via silver nanoparticles. Their extraordinary qualities and multipurpose uses pave the way for breakthroughs that could completely alter patient care, medicines, and diagnostics. Collaboration between scientific, governmental, and social spheres is necessary to realize their full potential. The biomedical applications of AgNPs offer a potential trajectory towards a future where healthcare is customized, transformative, and progressed by embracing possibilities, negotiating hurdles, and preserving ethical standards.

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CONFLICT OF INTEREST

The author declares no conflict of interest.

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