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Chitosan-Silver Nanoparticles: A Versatile Conjugate for Biotechnological Advancements

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ABSTRACT

Nano technology has emerged as a powerful field that enables the manipulation and control of matter at the nanoscale. One particular area of interest is the synthesis and application of silver nanoparticles (AgNPs) conjugated with chitosan, a biocompatible and biodegradable polysaccharide. This conjugate offers unique opportunities for various industries, particularly in biomedicine and environmental remediation. In the biomedical field, chitosan-silver nanoparticle conjugates exhibit significant potential as antimicrobial agents, wound dressings, and drug delivery systems. The combination of chitosan's biocompatibility and silver nanoparticles' antimicrobial activity provides an effective approach to combat infections and promote wound healing. Furthermore, the chitosan matrix can facilitate controlled release of therapeutic agents, enhancing their efficacy and reducing potential side effects. In environmental applications, chitosan-silver nanoparticle conjugates show promise for water purification, as they can effectively remove pollutants and disinfect water due to the antimicrobial properties of silver nanoparticles. Chitosan's ability to form gels and membranes further facilitates their use in filtration systems for wastewater treatment and environmental remediation. In conclusion, the conjugation of chitosan with silver nanoparticles represents a promising avenue in nano technology. This conjugate offers versatile applications in biomedicine and environmental remediation, leveraging the synergistic properties of both components. Further research and development are required to optimize the synthesis techniques, understand the mechanisms of action, and assess the long-term effects to ensure safe and effective utilization of chitosan-silver nanoparticle conjugates in various industries.

***Keywords:** Nanotechnology, Silver Nanoparticles, Chitosan, Drug delivery systems, Water Purification, Antimicrobial.*

INTRODUCTION

Nanotechnology can be defined as the science and engineering involved in the design, synthesis, characterization and application of materials and devices whose smallest functional organization in at least one dimension is on the nanometer scale (one-billionth of a meter[1]. In the past few years, nanotechnology has grown by leaps and bounds, and this multidisciplinary scientific field is undergoing explosive development. It can prove to be a boon for human health care, because nanoscience and nanotechnologies have a huge potential to bring benefits in areas as diverse as drug development, water decontamination, information and communication technologies, and the production of stronger, lighter materials[2].

The term "nanotechnology" was first defined by Tokyo Science University, Norio Taniguchi in 1974. 'Nanotechnology' mainly consists of the processing of, separation, consolidation, and deformation of materials by one atom or one molecule[3]. Nanoparticles that are defined to have at least their dimensions in the range of 1–100 nm have received steadily growing interest as a result of their unusual properties, arrangement to form superstructures and applications superior to their bulk counterparts. The nanoparticles are unlike bulk counterparts; their characteristics properties are governed by the rules of quantum mechanics rather than classical physics[4].

Depending on the overall shape these materials can be 0D, 1D, 2D or 3D[5]. The importance of these materials realized when researchers found that size can influence the physio-chemical properties of a substance e.g., the optical properties. These NPs showed characteristic colors and properties with the variation of size and shape, which can be utilized in bioimaging applications. For instance, A 20-nm gold (Au), platinum (Pt), silver (Ag), and palladium (Pd) NPs have characteristic wine-red color, yellowish gray, black and dark black colors, respectively[6].

Classification of NPs

Nanoparticles (NPs) are broadly divided into various categories depending on their morphology, size and chemical properties. Based on physical and chemical characteristics, some of the well-known classes of NPs are given as below.

Carbon-based NPs

Fullerenes and carbon nanotubes (CNTs) represent two major classes of carbon-based NPs. Fullerenes contain nanomaterial that are made of globular hollow cage such as allotropic forms of carbon. They have created noteworthy commercial interest due to their electrical conductivity, high strength, structure electron affinity, and versatility[7]. These materials possess arranged pentagonal and hexagonal carbon units, while each carbon is sp2 hybridized. Some of the well-known fullerenes consisting of C60 and C70 with the diameter of 7.114 and 7.648 nm, respectively. CNTs are elongated, tubular structure, 1–2 nm in diameter[8]. These can be predicted as metallic or semiconducting reliant on their diameter telicity[9].

Graphite nanoparticle (GNP) is an example of carbon-based NPs is ideal precursor to produce both homogeneous graphene quantum dots (GQDs) without any oxygen functional groups and GOQDs after an oxidation process[10].

Ceramics NPs

Ceramics NPs are inorganic nonmetallic solids, synthesized via heat and successive cooling. They can be found in amorphous, polycrystalline, dense, porous or hollow forms[11]. Therefore, these NPs are getting great attention of researchers due to their use in applications such as catalysis, photocatalysis, photodegradation of dyes, and imaging applications[12].

Semiconductor NPs

Semiconductor materials possess properties between metals and nonmetals and therefore they found various applications in the literature due to this property[13,14]. Semiconductor NPs possess wide bandgaps and therefore showed significant alteration in their properties with bandgap tuning. Therefore, they are very important materials in photocatalysis, photo optics and electronic devices[15]. As an example, variety of semiconductor NPs are found exceptionally efficient in water splitting applications, due to their suitable bandgap and band-edge positions[16].

Metal NPs

Metal NPs are purely made of the metal's precursors. Due to well-known localized surface plasmon resonance (LSPR) characteristics, these NPs possess unique optoelectrical properties. NPs of the alkali and noble metals i.e. Cu, Ag and Au have abroad absorption band in the visible zone of the electromagnetic solar spectrum. The facet, size and shape-controlled synthesis of metal NPs is important in present day cutting-edge materials[17]. Due to their advanced optical properties, metal NPs find applications in many research areas.

Silver Nanoparticles

Silver has long been known to exhibit a strong toxicity to a wide range of 116 micro-organisms for these reasons silver-based compounds have been used extensively in many bactericidal applications[18]. Several salts of silver and their derivatives are commercially employed as antimicrobial agents.

The bactericidal effect of silver ions on microorganisms is very well known; however, the bactericidal mechanism is only partially understood. It has been proposed that ionic silver strongly interacts with thiol groups of vital enzymes and inactivates them[19]. Experimental evidence suggests that DNA loses its replication ability once the bacteria have been treated with silver ions. Other studies have shown evidence of structural changes in the cell membrane as well as the formation of small electron-dense granules formed by silver and sulfur[20].

Silver ions have been demonstrated to be useful and effective in bactericidal applications, but due to the unique properties of nanoparticles nanotechnology presents a reasonable alternative for development of new bactericides. Metal particles in the nanometer size range exhibit physical properties that are different from both the ion and the bulk material. This makes them exhibit remarkable properties such as increased catalytic activity due to morphologies with highly active facets[21]. We can apply several electron microscopy techniques to study the mechanism by which silver nanoparticles interact with these bacteria. We can use high angle annular dark field (HAADF) scanning transmission electron microscopy (STEM), and developed a novel sample preparation that avoids the use of heavy metal based compounds such as OsO4. High resolutions and more accurate X-ray microanalysis were obtained[22].

The development of new resistant strains of bacteria to current antibiotics[23] has become a serious problem in public health; therefore, there is a strong incentive to develop new bactericides. Bacteria have different membrane structures which allow a general classification of them as Gram-negative or Gram positive. The structural differences lie in the organization of a key component of the membrane, peptidoglycan. Gram negative bacteria exhibit only a thin peptidoglycan layer (~2–3 nm) between the cytoplasmic membrane and the outer membrane; in contrast, Gram-positive bacteria lack the outer membrane but have a peptidoglycan layer of about 30 nm thick Silver compounds have also been used in the medical field to treat burns and a variety of infections[24]. Several salts of silver and their derivatives are commercially employed as antimicrobial agents[19]. Commendable efforts have been made to explore this property using electron microscopy, which has revealed size dependent interaction of silver nanoparticles with bacteria[18]. Nanoparticles of silver have thus been studied as a medium for antibiotic delivery, and to synthesize composites for use as disinfecting filters[21] and coating materials. However, the bactericidal property of these nanoparticles depends on their stability in the growth medium, since this imparts greater retention time for bacterium– nanoparticle interaction. There lies a strong challenge in preparing nanoparticles of silver stable enough to significantly restrict bacterial growth[25].

Polymeric NPs

These are normally organic based NPs and, in the literature, a special term polymer nanoparticle (PNP) collective used for it. They are mostly nanospheres or nanocapsular shaped[26]. The former are matrix particles whose overall mass is generally solid and the other molecules are adsorbed at the outer boundary of the spherical surface. In the latter case the solid mass is encapsulated within the particle completely[27]. The PNPs are readily functionalize and thus find bundles of applications[28].

Polymeric nanoparticles can be synthesized from natural and synthetic polymers. They are used owing to their stability and ease of surface modification. Biopolymeric nanoparticles have added advantages, like availability from marine (chitin and chitosan) or agricultural (cellulose, starch, pectin) resources, biodegradability, biocompatibility and nontoxicity. Biodegradable polymers such as chitosan are studied mainly as delivery systems for controlled release of active ingredients, stabilization of biological molecules like proteins, peptides or genetic material[29].

Nanochitosan

Chitosan is a modified biopolymer, derived by partial deacetylation of chitin. It consists of alternating units of (1 → 4) linked N-acetyl glucosamine and glucosamine units. It is a white, hard, inelastic and nitrogenous polysaccharide[30]. Chitosan finds multifaceted applications due to its nontoxicity, biodegradability and antimicrobial properties. It is used in biomedical industries, agriculture, genetic engineering, food industry, environmental pollution control, water treatment, paper manufacture, photography and so on[31].

The transformation of chitin into chitosan is achieved by deacetylation. The process can be either chemical, using a strong solution of sodium hydroxide (25–50%) and high temperature (90–120 ºC), or biochemical, using deacetylases. According to the conditions used in the deacetylation reaction, the resulting chitosan polymers will have different lengths, and also different remaining acetyl residues. This translates into a large range of molecular weights, from 300 to over 1000 kD. Moreover, the degree of acetylation of chitosan, ranging from 5 to 70%, has a strong influence on physicochemical properties such as viscosity and solubility[32].

Chitosan nanoparticles (CSNP) have the characteristics of chitosan and the properties of nanoparticles such as surface and interface effect, small size and quantum size effects[33]. CS-NPs have been prepared by several approaches, such as ionotropic gelation, microemulsion, emulsification solvent diffusion, polyelectrolyte complex and reverse micellar method[34]. Chitosan NPs are characterized by their physiochemical properties. These include biocompatibility, biodegradability, mucoadhesive character, absorption enhancing capability and in-situ gelling property.

Chitosan nanoparticles (CS-NPs) have exhibited improved biological activities such as antimicrobial[35], anticancer[36,37,] anti-inflammatory and antioxidant activities[38,39]. Chitosan NPs are effective in drug delivery and enhance the therapeutic efficacy of the drugs. They are used in ocular drug delivery due to its in-situ gelling properties and mucoadhesive character. They are used in oral drug delivery as it opens the tight junctions of the mucosal membrane and enhances absorption. Their positive charge makes them helpful in pulmonary drug delivery. They increase the permeability of various drugs making them available for nasal delivery. They enhance the absorption of hydrophilic molecules thereby helping in mucosal drug delivery. They act as an adjuvant in vaccine delivery. These have been found to be effective in cancer therapy[40].

Chitosan nanoparticles have shown anticancer activity *in vitro* and *in vivo* has been suggested that chitosan nanoparticles dose-dependent tumor suppression was correlated with the inhibition of tumor angiogenesis. Also, Chitosan nanoparticles can be used to deliver siRNA targeting key components of tumor metabolism. Due to their low or non-toxicity, chitosan nanoparticles and their derivatives can serve as a novel class of anti-cancer drug[41].

Chitosan nanoparticles can be used as carriers in the controlled drug delivery of doxorubicin, an anticancer drug used for the treatment of several tumors[42]. Doxorubicin can be toxic at some points and to protect patients from doxorubicin side effects were developed chitosan nanoparticles drug delivery system. It is possible to encapsulate and deliver doxorubicin with reduced side effects. The chitosan oligosaccharide conjugated with biodegradable doxorubicin with farther high efficiency in the tumor growth suppression because of higher cellular uptake[43].

Vignesh et al. prepared chitosan ascorbate NPs for the inhibition of cervical cancer. They performed various in vitro and in vivo studies and found that these NPs reduced the viability of the cervical cancer cells without affecting the viability of the normal human cells. So, this proves that these NPs are a potential system for treatment of cervical cancer[44]. Ana Vanessa et al used epidermal growth factor receptor-targeted chitosan NPs for the delivery of cisplatin for the treatment of cisplatin resistant and sensitive lung cancer models. They performed in vitro and in vivo studies and found that this system enhanced the tumor inhibition efficacy but was surprisingly more effective is cisplatin-resistant tumors[45].

Application of chitosan silver nanoconjugate

The application of nanotechnology in the field of biotechnology has revolutionized numerous areas, enabling advancements in drug delivery, tissue engineering, biosensing, and agriculture. Among the various nanomaterials explored, the conjugation of chitosan with silver nanoparticles (CS-AgNPs) has emerged as a promising platform with versatile applications. This conjugate combines the biocompatibility and controlled release properties of chitosan with the antimicrobial and catalytic capabilities of silver nanoparticles, opening up new opportunities for innovative biotechnological solutions[46].

Chitosan, derived from chitin, is a naturally occurring biopolymer known for its biocompatibility, biodegradability, and non-toxic nature. It has been extensively studied for biomedical and agricultural applications due to its unique properties, such as mucoadhesiveness, controlled release, and bioactivity modulation. On the other hand, silver nanoparticles possess excellent antimicrobial properties, high surface area-to-volume ratio, and enhanced catalytic activity, making them highly sought-after for a range of applications[47].

The conjugation of chitosan with silver nanoparticles offers several advantages. Firstly, chitosan provides a stable matrix for the nanoparticles, preventing aggregation and ensuring their sustained release. This controlled release capability is particularly valuable in drug delivery systems, where the sustained release of therapeutic agents can improve efficacy and reduce side effects. Secondly, the combination of chitosan's biocompatibility with the antimicrobial activity of silver nanoparticles makes CS-AgNPs an attractive candidate for wound healing, tissue engineering, and infection control. The antimicrobial properties of silver nanoparticles help prevent infections and promote tissue regeneration. Furthermore, CS-AgNPs have demonstrated potential in biosensing applications, where the catalytic properties of silver nanoparticles enable sensitive and selective detection of target analytes[48].

Several studies have investigated the application of CS-AgNPs in biotechnology. For instance, a study by[49] demonstrated the successful synthesis of CS-AgNPs and their application in the controlled release of an anticancer drug. The results showed enhanced drug release profiles and improved cytotoxicity against cancer cells. In another study by Mishra et al.[50], CS-AgNPs were utilized as a wound dressing material, exhibiting excellent antimicrobial efficacy against both Gram-positive and Gram-negative bacteria. These examples highlight the potential of CS-AgNPs in biomedical applications.

In agriculture, CS-AgNPs have been explored for their antimicrobial properties in crop protection and food preservation. A study by Elbagory et al.[51] demonstrated the inhibitory effect of CS-AgNPs against common plant pathogens, providing an eco-friendly alternative for disease management in agriculture. Furthermore, CS-AgNPs have shown potential in extending the shelf life of fruits and vegetables by inhibiting the growth of spoilage microorganisms[52].

CONCLUSION

In conclusion, the conjugation of chitosan with silver nanoparticles presents a versatile and promising platform for biotechnological applications. The unique properties of chitosan and silver nanoparticles synergistically contribute to improved drug delivery systems, wound healing, tissue engineering, biosensing, and agricultural practices. The application of CS-AgNPs in biotechnology holds great potential for addressing current challenges and advancing various fields, paving the way for innovative and sustainable solutions.

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Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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