Retrospecting Nanoparticles For Optimal Antimicrobial Potential: A Brief Review

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ABSTRACT

Nanotechnology comprises of creation of nanoscale particles by up scaling or downscaling minor or major materials, respectively. Nanoparticle, by convention, size in the range of 1 to 100 nm in size. It explores the electrical, optical, and magnetic potential, along with structural properties at molecular and atomic level. It has the capacity to revolutionize medical and biotechnology tools and methods for portable, economical, and easy to use applications. This study aims to present an overview of nanoparticles, with special reference to their mechanism of biosynthesis and their types. Nanoparticles can be synthesized chemically or biologically with different protocols either aggregating ionic particles or breaking down larger pieces into smaller ones. Metallic nanoparticles that have significant role in industries and are of different types, namely, Gold, Silver, Iron, Alloy, magnetic etc.

Key word: Antibacterial activity, Silver Nanoparticles, Concentration, Mechanism of nanoparticles, Applications of Nanoparticles

INTRODUCTION

Nanoparticles are being used for many industrial purposes, such as fuel batteries for energy storage ,cosmetics, textile, optical devices, antibiotic, electronics, biosensor technology, biological labelling and cancer treatment. Nanoparticles have achieved reasonable attention in recent years because of their exceptional properties like antibacterial activity, resistance to oxidation and improved thermal conductivity.

Nanotechnology is an emerging field of science which performs synthesis resulting in development of various nanomaterials. Nanoparticles can be defined as molecules ranging in size from 1-100 nm and their size may differ due to the bulk material used for production. Currently, various metallic nanomaterials are being produced using copper, zinc, titanium, magnesium, gold, alginate and silver as starting materials. Nanoparticles are produced for diverse applications, ranging from medical field to various branches of industry such as solar and oxide fuel batteries for energy storage, or to materials of everyday use such as cosmetics or clothes[1].

Antimicrobials are agents that act against bacteria (antibacterial), viruses (antiviral), fungi (antifungal/antimycotic), or protozoa (antiprotozoal). Amongst these, antibacterial agents are the most widely explored and studied class of antimicrobials. Pathogens causing lethal or health-damaging diseases could belong to both Gram-positive, especially methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus faecium* (VRE), and drug-resistant *Streptococcus pneumoniae*, and Gram-negative bacteria, namely multidrug-resistant *Acinetobacter baumannii* (MRAB), carbapenem-resistant *Enterobacteriaceae* (CRE), and *Pseudomonas aeruginosa*, display resistance to multiple drugs and are of serious concern.[5]

ANTIMICROBIAL NATURE OF NANOPARTICLES

The ability of nanoparticle efficacy against antibiotic resistant strains of bacteria belongs to their small size. Because of the nano scale, particles can behave as interfering molecules that interact with a cell allowing them to easily penetrate the cell membrane and interfere in vital molecular pathways provided the chemistry is feasible.[4]

Nanoparticles have been studied extensively for their antimicrobial properties especially against super bug bacteria[2][3]. There are certain characteristics of that make them nanoparticles strong candidates as a traditional antibiotic drug alternative. They have a high surface area to volume ratio, that increases their contact area with target organisms.[2][3] Furthermore, they could be generated from polymers, lipids, and metals.[2] Also, a group of chemical structures like fullerenes and metal oxides, allow various types of chemical functionalities.

TYPES OF NANOPARTICLES EXHIBITING BIOCIDAL NATURE

Classification of nanoparticles can be made in different types according to the size, morphology, physical and chemical properties. Some of them are carbon-based, ceramic, metal, semiconductor, polymeric and lipid-based nanoparticles.

Carbon-Based Nanoparticles

Carbon-based nanoparticles are made of two main types of material: carbon nanotubes (CNTs) and fullerenes. CNTs are basically graphene sheets rolled into a tube. CNTs are mainly used for the structural reinforcement as they are 100 fold stronger than steel. CNTs can be classified into single-walled carbon nanotubes (SWCNTs) and multi-walled carbon nanotubes (MWCNTs) based on the channels encompassed in the structure. CNTs are thermally conductive throughout their length and non-conductive across the tube. Fullerenes are the allotropes of carbon containing a hollow cage shape of sixty or more carbon atoms. Buckminsterfullerene looks like a hollow football and contains the structure of C-60. The carbon units in these structures have a pentagonal and hexagonal arrangement. They are commercially used due to properties like electrical conductivity, stable structure, high strength and electron affinity.

Ceramic Nanoparticles

Ceramic nanoparticles are made up of oxides, carbides, carbonates and phosphates and exhibit high heat resistance and chemical inertness. These nanoparticles are used in applications like photo catalysis, photo degradation of dyes, drug delivery and imaging. They also perform as efficient drug delivery agents, which is achieved by controlling ceramic nanoparticles characteristics like size, surface area, porosity, surface to volume ratio and more. These nanoparticles have been used effectively as a drug delivery agents to cure a number of diseases like bacterial infections, glaucoma and cancer.

Metal Nanoparticles

Metal nanoparticles are prepared from metal precursors by up scaling approach. These nanoparticles may be synthesized by electrochemical, chemical or photochemical method. In chemical methods, the metal nanoparticles are synthesized by reducing the metal-ion precursors in solution using chemical reducing agents. These nanoparticles can adsorb to small molecules and have high surface energy.

Metal nanoparticles have extensive applications in research areas like in detection and imaging of biomolecules, environmental and bio-analytical applications. Gold nanoparticles are used to coat the bio specimen before analysing in Scanning electron Microscopy (SEM). The metal nanoparticles enhance the electronic stream, which helps us to get high contrast and quality SEM images.

Semiconductor Nanoparticles

Semiconductor nanoparticles have properties of both metals and non-metals. They are found in the periodic table in groups II-VI, III-V or IV-VI. Their applications include photo catalysis, electronics devices, photo-optics and water splitting applications. Some examples of semiconductor nanoparticles are GaN, GaP, InP, InAs from group III-V, ZnO, ZnS, CdS, CdSe, CdTe are II-VI semiconductors and silicon and germanium are from group IV.

Polymeric Nanoparticles

Polymeric nanoparticles are organic based nanoparticles that are biodegradable and biocompatible. Depending upon the method of preparation, they have different shape like nanocapsular and nanosphere. A nanosphere particle has a beaded matrix-like structure whereas the nanocapsular particle having core-shell morphology. Advantages of polymeric nanoparticles are protection of drug molecules, availability to combine therapy and imaging, specific targeting and controlled drug release. They have applications in drug delivery and diagnostics.

Lipid-Based Nanoparticles

Lipid nanoparticles are spherical with a diameter range of 10 to 100nm[6][7]. The core comprises of lipid and a matrix containing soluble lipophilic molecules. The outer core of these nanoparticles is stabilized by surfactants and emulsifiers. They have application biomedical fields in form of drug carrier, delivery agents and RNA release in cancer therapy.

ANTIBACTERIAL MECHANISIM OF NANOPARTICLES

With increasing use of NPs in medical field, research on antibacterial mechanisms of NPs has been gaining higher significance. Metal NPs can interfere with the metabolic activity of bacteria.[34] This property has provided the NPs an advantageous capacity to eliminate pathogenic bacteria and cure diseases. NPs can penetrate biofilms for practical application to inhibit biofilm formation [35]. This property is beneficial for many medical fields, especially in dental healthcare industry. Studies at genetic level have demonstrated Ag-inhibited expression of genes.[35]

In order to attain high antibacterial effect, NPs need to be in direct contact with bacterial cells. This can occur through electrostatic attraction, van der Waals forces and receptor–ligand and hydrophobic interaction. After crossing the bacterial membrane and NPs interfere in the metabolic pathway, affecting the morphology and function of the cell membrane. The NPs can also interact with host macromolecules and organelles like DNA, lysosomes, ribosomes and enzymes. This can cause deleterious effects in form of oxidative stress, heterogeneous alterations, cell membrane permeability, electrolyte imbalance, enzyme inhibition, protein deactivation and altered gene expression.

The interaction of NPs with the cell barrier

The bactericidal mechanism of NPs is dependent on the bacterial cellular components and structure. The principal defence barriers for bacteria are cell walls and membranes against external environment. They also play an important role in maintaining the bacterium morphology. For entry process, NPs use different adsorption pathways of cell membrane components of Gram-positive and Gram-negative bacteria.[36] Bacterial lipopolysaccharide (LPS) is a unique feature of Gram-negative bacterial cell wall that provides a negatively charged region suitable to bind NPs. Teichoic acid found in Gram-positive bacterial cell wall, however, allows NPs to be distributed along the bacterial cell membrane, preventing their aggregation. In general NPs exhibit greater lethal activity against Gram-positive bacteria than against Gram-negative bacteria, due to the cell wall components like LPS, lipoproteins, and phospholipids, which form a penetrative barrier. In contrast, Gram-positive bacterial cell wall contains a thin layer of peptidoglycan, teichoic acid and abundant pores through which foreign molecules like NPs can penetrate, resulting in cell membrane damage and cell death.

PARAMETERS AFFECTING ANTIMICROBIAL NANOPARTICLES

Concentration and size

The influence of NPs size and concentration for effective antimicrobial activity has been analysed for many NPs. Silver nanoparticles with variable size range have been evaluated for bactericidal activity at a concentration as low as 0.01 ppm [8]. The smallest-sized sphere shaped silver nanoparticles were found to be more efficient in terms of bactericidal activity as compared to larger silver nanoparticles of similar shape. This is due to the high surface to volume ratio of smaller-sized NPs which release more silver cations as compared to larger-sized particles [9]

Chemical composition

The chemical composition of the NPs decides their potency of antibacterial activity. The NPs like TiO_2, ZnO_2 and SiO_2 are shown to exhibit oxidative stress against *Bacillus subtilis* and *Escherichia coli*. The magnitude of biocidal activity for these compounds was found in ascending order from SiO_2 to TiO_2 to ZnO. The growth of *B. subtilis* was 90 % inhibited by 10 ppm concentration of ZnO NPs, while a similar inhibition was observed with 1000 and 2000 ppm of TiO_2 and SiO_2, respectively. Whereas, the inhibition effect of NPs on *E. coli* was partially at 10 ppm of ZnO NPs, it was 500 ppm for combined TiO_2 and SiO_2 NPs [10]. Further, the bactericidal activity was shown to be unaffected by the presence of light.

The shape of NP

Studies performed on NPs morphology have suggested that different shapes (spherical, elongated rod and truncated triangular) of silver nanoparticles have varying intensity of bactericidal activity. NPs bactericidal activity appears to get stimulated by the respective morphology of NPs. The shape-dependent activity was determined in the term of number of facets. The spherical NPs primarily have 100 facets, rod shaped NPs have 111 facets on side surface and 100 on end, truncated triangular NPs have 111 facets on top basal planes. The facets 111 are of high atom density that favour's antibacterial reactivity of NPs [11].

Target microorganisms

Many studies have reported that NPs showed greater biocidal activity against Gram-negative rod-shaped bacteria than Gram-positive cocci. The effect of silver nanoparticles on *E. coli* and *S. aureus* showed significantly higher activity against *E. coli* (minimum inhibitory concentration, MIC 3.3-3.6) than *S. aureus* (minimum inhibitory concentration, MIC greater than 33 nM). The difference in results correlate with the cell wall organization, as the cell wall composition of Gram-positive bacteria (*S. aureus*) consist of higher concentration of peptidoglycan [12]. However, another study revealed equal activity of ZnO NPs against both Gram-positive (*S. aureus*) and Gram-negative (*E. coli*) bacteria [10]. Whereas another study has reported ZnO NPs higher activity against *S. aureus* than *E. coli* and *P. aeruginosa* [13].

Photo activation

The NPs of TiO_2 showed activity against *E. coli* that significantly increases in synergism with UV radiation [14]. Further, it was reported that TiO_2 NPs has negligible activity against *S. aureus* without photo activation. On the other hand, ZnO NPs exhibit escalating activity after photo activation by UV radiation including visible light [15,16]. It has also been demonstrated that the photo activation with blue light of these NPs enhances their activity by enhancing reactive oxygen species (ROS) production, with prominent effect in ZnO NPs [17]. The fact needs to be confirmed that bacterial incubation with NPs in dark condition has no effect on surviving of microorganisms [10].

COMMERCIAL APPLICATION OF BIOCIDAL NANOPARTICLES

Applications of nanomaterials in biology or medicine include fluorescent biological labels [18,19,20], drug and gene delivery [21,22], bio analysis of pathogens [23], detection of proteins [24], probing of DNA structure [25], tissue engineering [26,27], hyperthermia[28], separation and purification of biological molecules and cells [29], Magnetic Resonance Imaging contrast enhancement [30], phagokinetic studies [31]

Nanomaterials are generally considered suitable for bio-tagging or labelling due to their consistent size domain as proteins targets. However, size poses just one of the factors for nanoparticles to be used as biological tags. The biological layer acting as an interface needs to be attached to the nanoparticle in order to interact with biological target. Such biological coatings include antibodies, biopolymers like collagen or monolayers of small molecules that give the biocompatibility property to the nanoparticles. Besides these, optical detection techniques that are wide spread in biological research, impose a pre-requisite for nanoparticles to either fluoresce or change their optical properties.

Nano-biomaterial generally contain a core made of nano-particles. However they can be used as convenient surfaces with molecular assembly, and may be composed of inorganic or polymeric materials. Other forms include nano-vesicles surrounded by a membrane or a layer. The nano-biomaterial shape is mostly spherical but can be cylindrical, plate-like and made of other shapes. Shape and size distribution may affect penetration through a pore structure of a cellular membrane whenever required. These become more critical when quantum-sized effects are used to regulate material properties. Efficient fluorescent probes emitting narrow light spectrum in a wide range of wavelengths can be achieved with precise control of the average particle size. An immediate application of these probes is illustrated by biomarkers with large range and defined colours. The nano-biomaterial core can be multi-layered to exhibit multifunctional nature of the nanomaterials. This can be achieved by combining magnetic and luminescent layers for the functions of concentration and detection of the particles, respectively.

As seen in Silica based nanomaterials, the core particle is protected by several monolayers of inert material. Organic molecules can also be coated to the surface of the particle by adsorption for creating multiple biocompatible layers. Further functionalization can be achieved by the addition of linker molecules containing reactive groups. One group is used to anchor the linker to the nanoparticle surface, while the other group is used to bind molecules like bio compatibles (dextran), antibodies, fluorophores, depending on the function required for the application.

FUTURE DIRECTION

Given the current scenario, the majority of industrial nanoparticle applications in medicine are developed towards drug delivery. Nanoparticles have provided high photo-stability by replacing organic dyes. Some of the fascinating applications that nanotechnology is gaining significance is remotely controlling the functions of nano-probes, as seen in driving magnetic nanoparticles to the tumour locations and delivering the drug load or by thermal treatment aimed to destroy the targeted tissue. The future goals of nanotechnology is to enhance multifunctionality and regulation of nano-machines by external or local stimuli.

CONCLUSION

Nanotechnology depends on its basic blocks of nanomaterials that are constantly evolving the fields of energy, health care, environment and agriculture. Nanoparticle based technologies have great potential to convert waste materials into biologically active or promising deliverable substances. Since ages, nanomaterials have been successfully demonstrated as antiseptic agents in form of metal nanoparticles. With various type of ligand addition, they have expanded their zone of applications. Antibacterial nature of nanomaterials is a promising alternative to replace current antibiotics and the resultant drug-resistance problems caused. They also provide another route to reduce environmental pollution of medical waste. The field of nanotechnology is yet to expand and statistically growing in exponential pattern. This field has potential to provide higher assistance to the medical technology through the novel antibacterial composites that are being experimentally tested.

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