Antimicrobial Properties of Nanoparticles (NPS)

Received for publication, December 3, 2019, and in revised form, January 5, 2020

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Abstract

With the help of nanoparticles treatment of diseases without any side effects can be achieved with the help of nanotechnology. The devices operating at nanoscale range such as nanoparticles, paves the path for a new method for imaging, diagnosis and therapy. Nanoparticles have antimicrobial properties which can locally destroy bacteria, without doing any harm to the surrounding tissues. This review focuses on the antimicrobial effects of nanoparticles.

Keywords: Nano particles, nanoscale, antimicrobial properties

Introduction

Antibacterial activity is related to compounds that locally kill bacteria or slow down their growth, without being in general toxic to surrounding tissues. Chemically modified natural compounds are the most current antibacterial agents [1], viz. β-lactams and carbapenems. Sometimes aminoglycosides – a pure natural product and sulfonamides – purely synthetic compounds are often used. Antibacterial agents are used to fight bacterial diseases. These agents are classified as bactericidal which kill bacteria or slows down bacteria growth [2]. With the wide use of antibacterial drugs, the emergence of bacterial resistance has become a common and a major problem .Resistance- which is a common evolutionary problem taking place during , for example, antibiotic therapy which leads to diseases which are inheritable. Moreover, horizontal gene transfer through conjugation, transduction or transformation is a probable way for building up resistance [3]. These antibacterial resistant strains are known as superbugs which contribute to the emergence of diseases that were in perfect control for several years. Tuberculosis is a prominent example of disease caused by bacterial strains which is resistant to treatment of previous antibacterial treatments. Multidrug-resistant (MDR-TB) tuberculosis occurs every year at a rate of half a million new cases worldwide [4]. Delhi metallo-β-lactamase-1 (NDM-1), a newly identified enzyme, which is responsible for bacterial resistance to a broad range of β – lactam antibacterial, and it seems that most isolates with NDM-1 enzyme are resistant to all standard intravenous antibiotics for treatment of severe infections [5]. Bacteria develop resistance to many conventional procedures of antibacterial activities which is a major problem around the world. Secondary effects (side effects) of such prevailing antibacterial treatments are a major concern and as the bacteria develop resistance to these treatments, high doses of these drugs are being administered inside the body which causes serious toxic effects to the body and dew to this problems the search for alternative antimicrobial agents such as NPs are in vogue. Nanosized particles as well as nanoparticles which are used to deliver drugs have proven themselves effective in treating microbial diseases and also antibiotic-resistance ones *in-vitro* as well as animal models. NPs offer improved properties because they have high surface area to volume ratio, which results into a new mechanical , chemical,

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electrical, optical, magnetic, electro-optical, and magneto-optical properties that NPs that are much different from their bulk properties [6].NPs have interesting properties which can control bacteria and are discussed below.

Multifunctional Nano-particles

Nanoparticles are small sized particles around (1-100nm) in size. Nanometer-sized particles are in the same range of dimension as antibodies, membrane receptors, nucleic acids and proteins, amongst other biomolecules. These unique features alone with their attractive surface: volume ratio makes nano particles a very powerful tool for combating bacteria, their diagnosis and therapy[7,8].Nanoparticles have many advantages over the other available procedures for disinfecting bacteria and it is gaining popularity in the market nowadays[9]. Some types of nanoparticles are described below-

Liposomes- They are phospholipid vescicles (50-100nm). They have a phospholipid bilayer which are very similar to the other biological membranes and it consists of an aqueous internal phase. They are classified as multi-, oligo-, or uni-lamellar, according to their size and number of layers. They are used to transport hydrophilic drugs which are being entrapped into their aqueous interior and hydrophobic drugs dissolved in their membrane [10].

Dendrimers- These are highly branched synthetic polymers (<15nm) which consists of a centralized core, an internal region and numerous terminal groups which determine the characteristics of a dendrimer. Dendrimers are used to repair tissue-scaffolds which is due to their intrinsic drug properties. They are also excellent diagnosis-carrier agents [11].

Carbon nanotubes- Carbon nanotubes are formed of coaxial graphite sheets (<100nm) which are rolled into cylinders. These nanotubes are often obtained as – one graphite sheet or several concentric graphite sheets. They are very efficient heat conductors too. They are often used as bio-sensors because of their excellent semiconductor nature. They are water soluble and they are widely used as drug carriers and tissue repair scaffolds [12].

Quantum dots- They are of (2-10nm) in size. They are mostly colloidal fluorescent semiconductor nanocrystals. The central core consists of elements (CdSe, CdTe, Cds ,PbSe , Zns and Znse) or the elemts of the periodic tale group II-VI OR, III-V (GaAs , GaN, InP, and lnAs) and are overcoated with a layer of Zns. They are resistant to- photo bleaching, photo and chemical degradation. All these thongs make quantam dots very good agents for imaging, labels and bioassays [13].

Gold Nanoparticles- They are a type of metallic nanoparticles having sizes (<50nm).They have localized localized surface plasmon resonant properties. They have the property of absorbing light and emitting photons with same frequency in every directions. They detect numerous techniques such as optic absorption, fluorescence and electric conductivity and can act as excellent bio sensors [14].

Silver Nanoparticles- Silver nanoparticles are nanoparticles of silver of between 1 nm and 100 nm in size. While frequently described as being 'silver' some are composed of a large percentage of silver oxide due to their large ratio of surface-to-bulk silver atoms [15].

Multifunctional nanoparticles for drug and gene delivery-

Multifunctional drug delivery is a new emerging scientific technology but they are already in use for several *in vivo* studies with multifunctional nanoparticles. They provide an interesting prospect and a bright future of these novel nanoparticles. An excellent example of the effectiveness of these nanoparticles is the treatment of cancer which is done by Yang and co-workers. These scientists developed a multifunctional nano system combining magnetic nano crystals (MRI),with antibodies which are therapeutic and a chemotherapeutic drug doxorubicin. Multifunctional NPs are used for *in vivo* imaging and si RNA delivery and silencing tumors.

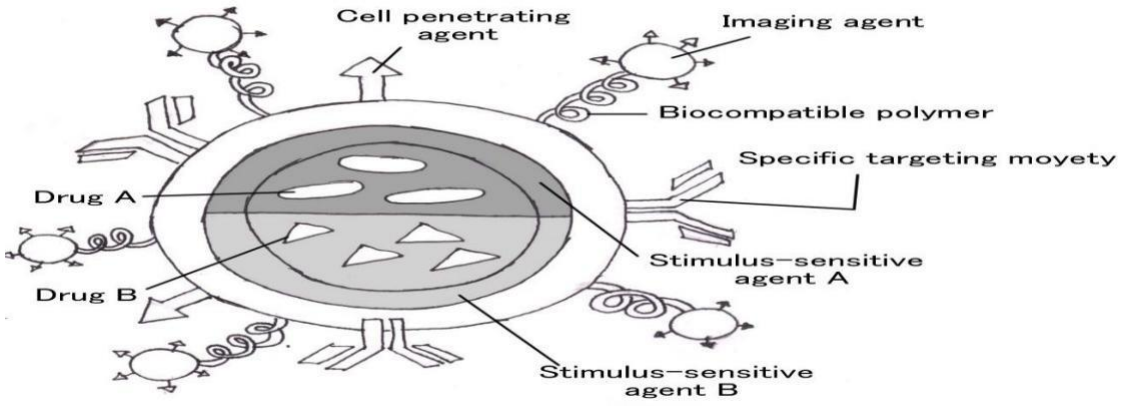

Fig. 1*- Multifunctional nanoparticles for drug delivery-* Multifunctional nanocarriers can combine a specific targeting agent (usually an antibody or peptide) with nanoparticles for imaging (such as quantum dots or magnetic nanoparticles), a cell-penetrating agent (e.g. the polyArg peptide TAT), a stimulus-sensitive element for drug release, a stabilising polymer to ensure biocompatibility (polyethylene glycol most frequently) and the therapeutic compound. Development of novel strategies for controlled released of drugs will provide nanoparticles with the capability to deliver two or more therapeutic agents (16)

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Properties of bacteria and their highly specific ways to destroy them

Role of cell wall- The bacterial cell wall provides strength and and many other protective properties to the cell [17]. According to the properties of the bacterial cell they can be divided into two groups- Gram negative(-) and Gam-positive(+) bacteria .There is a thick peptidoglycan(PG) layer is present in the walls of the Gram positive cells that are attached to techoic acids. Whereas, the cell wall of gram negative are more complex both structurally and chemically. In Gram-negative it contains a thin PG layer and an outer membrane. In Gram-Negative bacteria I provides resistance to various detergents and contains lipopolysaccharide, which is responsible for the negative charge of cell membranes and are also responsible for structural integrity and viability of the bacteria. The structure of the cell wall plays a very important role to tolerate the presence of NPs.

Role of the NP type and surface – Several additional factors including species sensitivity has the power to influence the susceptibility or tolerance of bacteria to NPs. Example, *E.coli(-)* is highly susceptible whereas *S.aureus* (+) and *B.subtilis* (+) are less susceptible to CuO NPs [18].

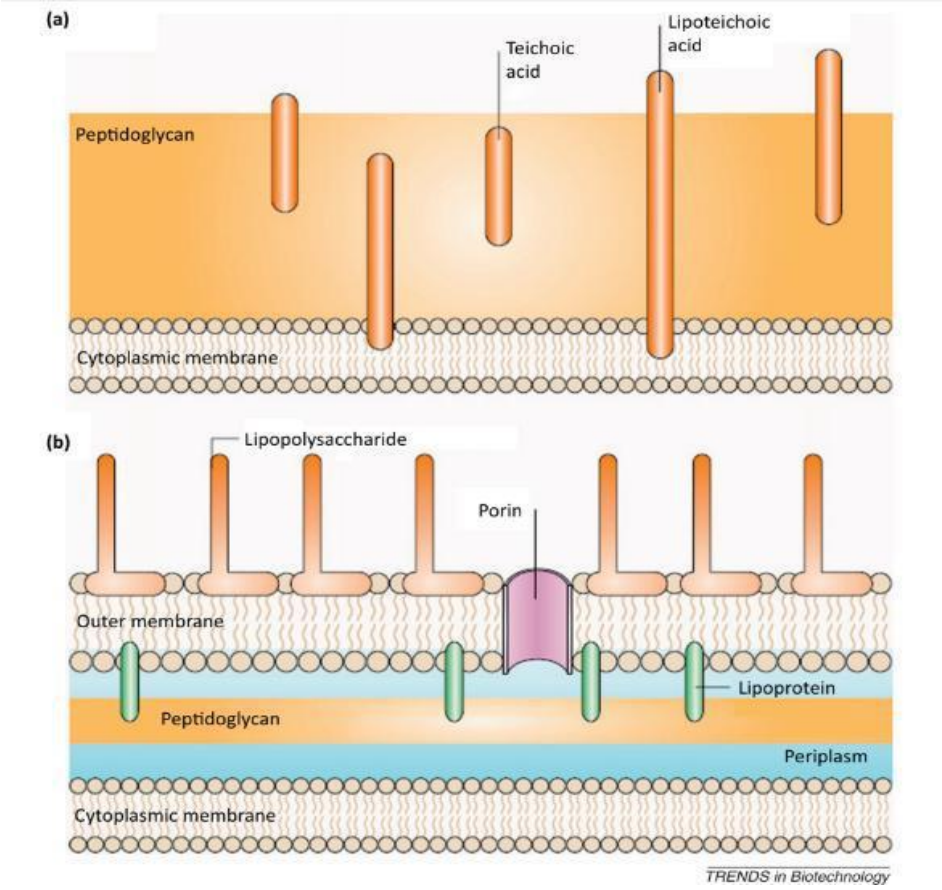

Fig-2 *Bacterial cell structure*. (a) A Gram-positive bacterial cell wall is composed of a thick and multilayered peptidoglycan (PG) sheath outside of the cytoplasmicmembrane. The teichoic acids, as seen, are connected to and embedded in the PG, and lipoteichoic acids extend into the cytoplasmic membrane. (b) A Gram-negativebacterial cell wall is composed of an outer membrane linked by lipoproteins to thin and single-layered PG.

The PG is placed within the periplasmic space that is formed between the outer and inner membranes. The outer membrane includes porins and lipopolysaccharide molecules [19].

Role of growth rate- NPs and antibiotics act better on fast growing bacterias than the slowly growing bacteria [20, 21] . Slow growing bacteria have stress-responsive genes so they can tolerate NPs. [22, 23] .Particular strain is the main determinant factor for antibacterial effects.

Role of biofilm formation- Bacteria which can produce biofilms can resist NPs and antibacterial drugs [viz.- S.aureus(+)] .A complex microbial community which are known as biofilms that form by secrection of a matrix and adhesion to a solid surface,that covers the total bacterial cell community. Biofilms formation gives a protection against pathogenetic bacteria against antibiotics and is solely resbonsible for the development of chronic infections [24].Most of the bacteria have negatively charged biofilm matrixes but *Staphylococcus epidermidis* (+) has a poly cationic film. The bioaccumulation and uptake of Ag NPs to the biofilms is directly proportional to the presence of Suwannee River fulvic acid (SFRA) [25]. But, in the absence of SRFA, Ag NPs can only impact to biofilms. In the other cases the viability of bacteria is unchanged. SRFA creates an intrinsic

antioxidant activity can protect the bacteria against the NPs from significant damage [26]. Concentration of Ag NPs are responsible for Ag NP uptake by marine biofilms and reduction of marine biofilms [27]. Colonization of new bacteria into the biofilms and decrease its development and succession may be prevented by the exposure of Ag NPs . The anti microbial activity of Mg F2 NPs have the capability to prevent biofilm formation of common pathogens such as E. coli and S. aureus [28]. Catherers modified by Mg F2 NP are able to restrict the biofilm formation of the bacteria significantly [29].They have also demonstrated that glass surfaces coated with ZnO NPs are able to produce reactive oxygen species (ROS) that interfere with *E.coli* and *S. aureus* biofilm formation [30].NPs with different surface coatings (ex with gold and silver) are called Supermagnetic iron oxide NPs (SPIONS) and shows the capacity to show highest activity against the biofilms [31, 32]

The toxicity of NPs against bacteria-Electrostatic interaction interactions helps the NPs to attach to the membrane of the bacteria to disrupt the integreity of the membrane [33]. Following the administration of NPs the nano-toxicity is generated by the induction of oxidative stress by free radical formation which is called the ROS (Reative Oxygen Species) . [34,35]

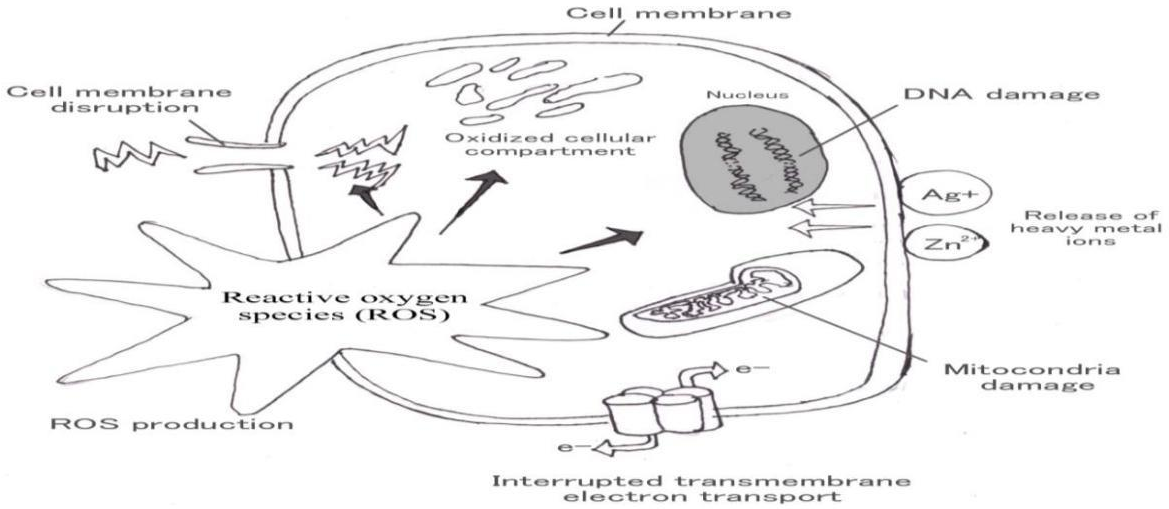

Figure-3 Mechanisms of toxicity of nanoparticles (NPs) against bacteria. NPs and their ions (e.g., silver and zinc) can produce free radicals, resulting in induction ofoxidative stress (i.e., reactive oxygen species; ROS). The produced ROS can irreversibly damage bacteria (e.g., their membrane, DNA, and mitochondria), resulting inbacterial death [45]

The TiO2 and Zno NPs have the capability of making frameshift mutations in *Salmonella typhimurium* (-), (TA 98 and TA 1537) [36]. The presence of S9 fractions in Zno NPs are responsible for the frameshift mutation. Internalization of NPs are activated by the S9 fraction which then generates the ROS that helps in making the frameshift mutation in bacteria. TiO2 NPs are toxic to *P. aeruginosa* (–), *E. hire (+), E. coli (–), S. aureus (+), and B. fragilis* (–), only under UV illumination and killed approximately all bacteria in 60 min. These NPs have combination of several factors such as temperature, aeration, pH, concentration of NPs and the concentration of bacteria (*E. coli*) determines the toxicity of NPs. The agglomeration can be decreased and toxicity can be increased by the high temperature, high aeration and low pH. The lower agglomeration provides more available surface area for interaction with bacterial membranes and for solubilization of copper ions, which leads to more toxicity [39]. Metallic and ionic forms of copper produce hydroxyl radicals that damage essential proteins and DNA [40]. Au NPs which are prepared in solution by using the citrate reducing method are photomutagenic against the *S. typhimurium* strain

TA102. The coexisting Au^{3+} ions and citrate are responsible for the photomutagenicity of Au NPs and it is not related to their intrinsic properties. In the presence of light the oxidation of Oxidation of Au^{3+} and decarboxylation of citrate induce the generation of free radicals that damage essential proteins and DNA [41].

Living organisms produce Biogenic Ag NPs, are co-operative effects with antibiotics such as erythromycin, chloramphenicol, ampicillin, and kanamycin against Gram-negative and Gram positive bacteria [42]. Biogenic Ag NPs with antibiotics has a very efficient antibacterial activity. Ampicilin, which damages the cell wall and helps to internalize NPs into the bacteria. Internalization of NPs makes NPs binds to DNA and inhibits the unwinding of DNA resulting to cell death. Titanium modified NPs are toxic to *E. coli* and *S. aureus* Ag NPs disrupt the membrane inegrity of bacteria and inhibit bacterial growth [43]. These above studies reveals the antibacterial activity of the NPs.

NPs against drug-resistant bacteria – The emergence of antibiotic resistance are a global concern for mankind. To destroy antibiotic resistanc bacteria requirres many expensive drugs which are very expensive as well as it has many toxic effects to the body. This problems can be tackled by the NPs (44).Four variants of silver carbon complexes (SCCs) with dwith various formulations including the micelles and NPs have great toxicity against medicalyy important pathogens such as *P. aeruginosa* (–), *B. cepacia* (–), methicillin-resistant *S. aureus*, multidrug-resistant *A.baumannii* (–), and *K.pneumoniae* (–) in the range of 0.5–90 mg/l (44). The growth of bio-defense bacteria such *as B. subtilis* and *Y. pestis* (-) are inhibited by SCCs [44].

Conclusion

Nanoparticles can be administered by parental, nasal, oral and occular routes. By attaching specific ligands to their surface, nano particles can be used for directing the drugs to specific targets. It also improves stability and therapeutic index and reduce toxic effects. Both active and passive drug targeting can be achieved by particle size and the surface characteristics of the nano particles. [45].Nano particles can also pave the way for treatment of diseases without the help of antibiotics resulting in less antibiotic resistance and ultimately will reduce the global concern for antibiotic resistance.

Acknowledgements-

I want to express my sincere thanks to Ankita Mukherjee and Manmata Dhara for helping me out in writing this review work.

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