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A Minireview: Nanomaterial as Antimicrobial Agents

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Abstract:

The design, synthesis, and application of substances and gadgets whose size and shape have been designed at the nanoscale can be defined as nanotechnology. Nanoparticles (NPs) are used for the manufacture of multiple applications of different nanoscale materials, especially in diagnostic and therapeutic diseases. The size of nanoparticles is proportionate to biomolecules and microbial cell structures, and it provides a medium for fine-tuning interactions between nanomaterial-bacteria through appropriate surface modification. An antimicrobial agent is any substance of natural or synthetic origin that explicitly kills or inhibits the production of microorganisms, causing just a little or no harm to superior organisms. The production of biofilms is a highly complex process in which microbe cells transmute from planktonic to sessile growth modes. The formation of

biofilms depends on the expression of genetic components (genes) that have contributed to the production of biofilms. The mode of action of NPs is poorly known, but metal ion release, oxidative stress induction and non-oxidative mechanisms are the mechanisms generally recognized. In this review, we discuss the antimicrobial resistances and biofilm development, mechanisms of action nanoparticles, antimicrobial nanorough surfaces. Applications in antibacterial therapies are also discussed.

Keywords: *nanoparticals, antibacterial, antibiofilm.*

1- Introduction:

Nanoparticles and nanostructured substances are an active research area and a techno-economic fabric with complete expansion in many fields of application. Because of the tunability of their physical-chemical features such as wettability, melting point, thermal conductivity and electrical, catalytic efficiency as well as light absorption, both forms of materials have gained popularity in technological evolution [1].

A nanometer (nm) is an International System of Units that can be expressed as $1\text{-}10^{-9}$ meters in length in scientific notation. Nanomaterials (NMs) are materials with internal or external nanoscale dimensional structures and at least one dimension with a length of 1-1000 nm; however, diameters in the range of 1 to 100 nm are typically known. There does not exist a single universally agreed definition for NMs. There is a difference of opinion between different organizations in describing NM [2].

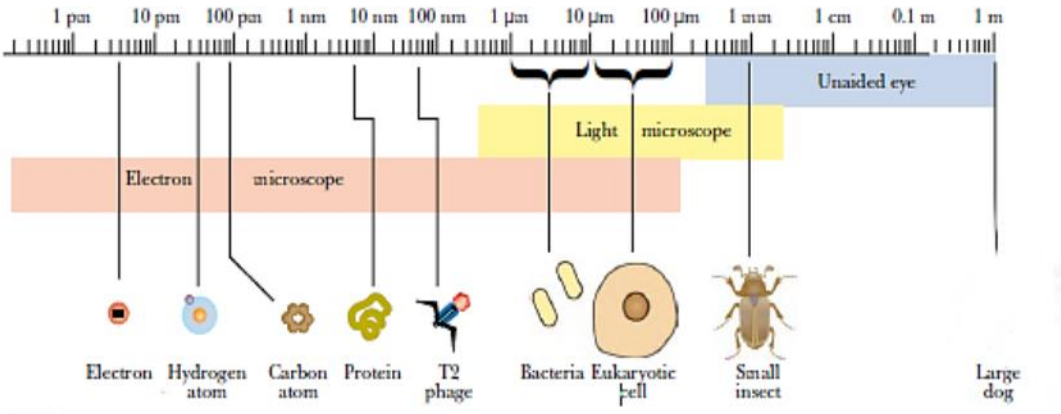


Figure (1) Nanoparticles size in compare with the microorganism and live organism [3]

NMs are referred to by many agencies and organizations such as (EPA) and (USFDA) as substances with At least one dimension in the variety of approximately (1 to 100 nm) and tend to be Phenomena that are dimension-dependent [4]. NMs are often referred to

by the International Organization for Standardization (ISO) as a substance with an dimension have external or surface structure of an internal nanoscale [5].

The term nanobiotic is used to describe nanomaterials which possess antimicrobial efficiency themselves or increase the antimicrobial activity of currently The term nanobiotic is used to describe nanomaterials which, on their own, possess antimicrobial efficiency or increase the antimicrobial activity of the treatments and compounds currently used [6]. The use of many of the antimicrobials currently on the market leads to harmful and acute side effects, a downside that can be resolved by the use of nanobiotics. The long-term consequences of exposure to such medication, combined with nanobiotics, remain to be seen as these threats have not yet been covered by clinical trials [7].

2- Antimicrobial Resistance and Biofilm Development

NMs introduce a broad variety of classes and applications of antimicrobials. Compared to small molecular antibacterial agents that display short-term efficiency and environmental toxicity, these NMs provide sustained antibacterial activity with negligible toxicity. One of the key problems with small molecular antibiotics is the creation of resistant species because of their unique goals of action, whereas nanomaterials physically kill cell membranes of the microbe's cause stopped the development of drug-resistance species [8]. Because of these benefits offered by nanomaterials, attempts have been made to apply these NPs to medical devices, fabrics, and textiles as contact surfaces, making them antimicrobial. The need to enhance the quality of life will be fulfilled by modern research, consecrated efforts, effective implementation and commercialization of antibacterial nanomaterials [9,10].

The predominant cause for chronic infections and death rates is bacterial infections. Due to their cost-efficiency and good results, the appropriate treatment for antibiotics has been tool for microbial infections. Nonetheless, various recearches have presented direct indecator about the widespread use of antimicrobial agents has contributed to the growth of multidrug-resistant bacterial strains. Indeed, due to the misuse of antibiotics, super-bacteria that are immune to almost all antimicrobial agents have recently formed. Studies provided (NDM-1) as a super-resistance gene [10] is found in bacterial cells. There are three bacterial targets for the main classes of antibiotics currently in use: synthesis of cell wall and translation and DNA replication machinery [11].

Regrettably, compared to any of these modes of operation, bacterial resistance may develop. Resistance mechanisms as a result of expression many enzymes that alter or degrade antibacterial agents, such as aminoglycosides and β-lactamases, the modification of cell ingredients such as vancomycin resistance of the bacterial cell wall and tetracycline resistance

of ribosomes, and the expression of efflux pumps that provide simultaneous resistance to various antimicrobial age groups [12,13]. Several pathways are used by these microorganisms to achieve multi-drug tolerance. The minimum inhibitory concentration (MIC) is the key pharmacodynamic (pd) parameter consist of antibacterial regimens and their design, since the discovery of antibacterial agents, although all assays in vitro test only the behavior of fixed antibiotic concentrations over time [14].

Owing to the different wall structure in Gram-negative bacteria, the antibacterial agent has had an effect on Gram-negative bacteria other than gram-positive, primarily on the outer membrane. The outer membrane acts as an important barrier to permeability that can exclude and barrier macromolecules (such as enzymes or bacteriocins) and hydrophobic many substances (i.e., Hydrophobic antibiotics). The property of large permeability membrane barrier related to the outer membrane, caused by the presence on the membrane surface of a particular lipopolysaccharide (LPS) layer. A lipid component consists of LPS molecules known as lipid A and a heteropolysaccharide hydrophilic chain that protrudes outward and provides a hydrophilic surface to the cell[15].Release of LPS is due to some external agents found in the outer membrane and other components or intercalate the membrane, allowing the integrity of the outer membrane to be eliminated. There is a concurrent failure of the permeability barrier function in both cases [16].

The antibacterial activity is associated with different compounds they all cooperate to slow down the growth or kill of bacteria without being harmful to the surrounding tissue. Moreover, chemically altered natural compounds are modern antibacterial agents[17]. B-lactams (as: penicillin) and cephalosporin, for example, were widely used. The agents can usually be classified as either bacteriostatic and decline the growth of bacteria, or bactericidal, killing bacteria. The antibacterial agents are being discovered to combat infectious diseases[18] However the production the resistance of bacteria to antibacterial tretment has progressed with their widespread use and manipulation, A widespread phenomenon that has been a key issue. Most commonly, bacterial resistance is focused on Processes of evolution that take place like:

1- Antibiotics enzymatic deactivation.

2- Diminished antibiotic permeability of the cell wall.

3- Changed antibiotic target sites.

4- Efflux pathways for antibiotic clearance [19].

5- Increased rate of mutation as a stress reaction [20].

These contribute to resistance that is inheritable. In addition, transfer of gene horizontally through conjugation, transformation or transduction may be a potential way of building up resistance.[21] Therefore since bacteria have built resistance to many traditional antibacterial agents, infectious diseases remain one of the world's biggest health challengesIn addition, the advancement of multiple drug resistance is not only a problem for traditional antimicrobial treatments, but also has Side effects which are harmful. Resistance to drugs put in place High-dose antibiotic administration, often creating unacceptable toxicity. This has encouraged the development of alternative bacterial disease management strategies [21]. Nanomaterials have been produced as new antimicrobial agents, among others. In particular, various groups of antimicrobial NPs and Nano sized antibiotic delivery carriers have shown their efficacy in the treatment of infectious diseases [22]. Why can proposals from NPs enhance the properties of conventional organic antibacterial treatment? One explanation is their broad surface-to-volume ratio, which results in the emergence of new magnetic, mechanical, optical, electrical, chemical, electro-optical and magneto-optical properties of nanoparticals that differ from their best-component properties.[23] In this situation, nanoparticals have been shown to be of interest in the battle against bacteria [24].

Most microbial species are contained in the biofilm, which also includes diverse species that react for one another and their surroundings. Biofilms are a particular microbial collection that like extracellular polymeric substances, relies on a extracellular products (EPSs) and solid surface [25]. The bacterial cell moves onto the roof reversibly, while the expression of EPSs contributes to an irreversible correlation. If the bacteria have settled, the flagellum of bacteria were stopped synthesis, and the bacteria redouble fastly, creating in the creation of biofilm as a mature. The bacteria are stuck with each other in this level, the creation of a barrier which can resist antimicrobial agents and provide a source of chronic systemic infections. The development of biofilms is therefore considered a significant threat to health [22,26]. In addition, superantigens may be produced by the bacterial cells inside biofilms to escape the immune system.

Therefore, bacterial infections remain a major problem amid The surplus of antimicrobial substances and many modern antibacterial drugs. Owing to their intrinsic tolerance in each antimicrobial substances and defenses of host, persistent infections linked to biofilms and planktonic bacteria are often hard to treat. In addition, antibiotics are less restrained from biofilm formation than the respective planktonic bacteria [27].

3- Antimicrobial Nanorough Surfaces

Surface chemistry and nanoscale topography, In terms of eukaryotic cells, it has been extensively researched, but is less understood in relation to bacterial cells. Also much promise

has been shown by the small number of studies so far. The aim of most nanorough surfaces in antibacterial is to prevent adhesion of bacteria cells and the formation of biofilm, the main reason of infection. The invasion of a bio-substances surface with bacterial cells is a significant challenge to the effectiveness of a medical product [28].

Although physical appeal to bacteria in nanoparticles is a required property, for nanomaterial surfaces it is an undesirable property. As an important material property in NPs, positive zeta potential has been established, In antibacterial, nanorough surfaces, but may need to be avoided. A material surface's positive zeta potential, or surface charge, can attract bacterial cells in the same method that nanoparticles are associate with the bacterial surface. Although NPs can destroy the bacteria, surfaces may be more actively colonized. Therefore to mitigate the reaction of negatively charged bacteria, surfaces material should preferably have a negative charge in the surface [29].

Other mechanisms associated with increased of nanoparticals as antibacterial activity, like increased release of ions, may also be similarly increased on nanorough surfaces because increased properties and functional of surface area. However, other specific mechanisms may control antibacterial properties of substances that do not have antibacterial properties on traditional topographic surfaces.

Due to the ability of the bacteria to more easily create a biofilm on the surface of the material in grooves or pits, micronscale roughness was established in biomaterial surfaces, as an undesired property. However, although not well understood, the interaction between nanorough surfaces and bacteria can theoretically reduce bacteria's adhesion interactions that could be electrostatic strengthened when a bacterium's cell wall may flush against a material surface are controlled by the components of the initial adhesion of bacteria mechanism. Because the stiffness of the cell wall, ruggedness on the nanoscale can to avoid near contact with the cell wall, and the material surface. A bacterial cell wall may not be able to adhere To the topography of a substance with surface features of a nanoscale, inhibiting the premature stages of bacterial cell adhesion, unlike a very flexible eukaryotic cell [30].

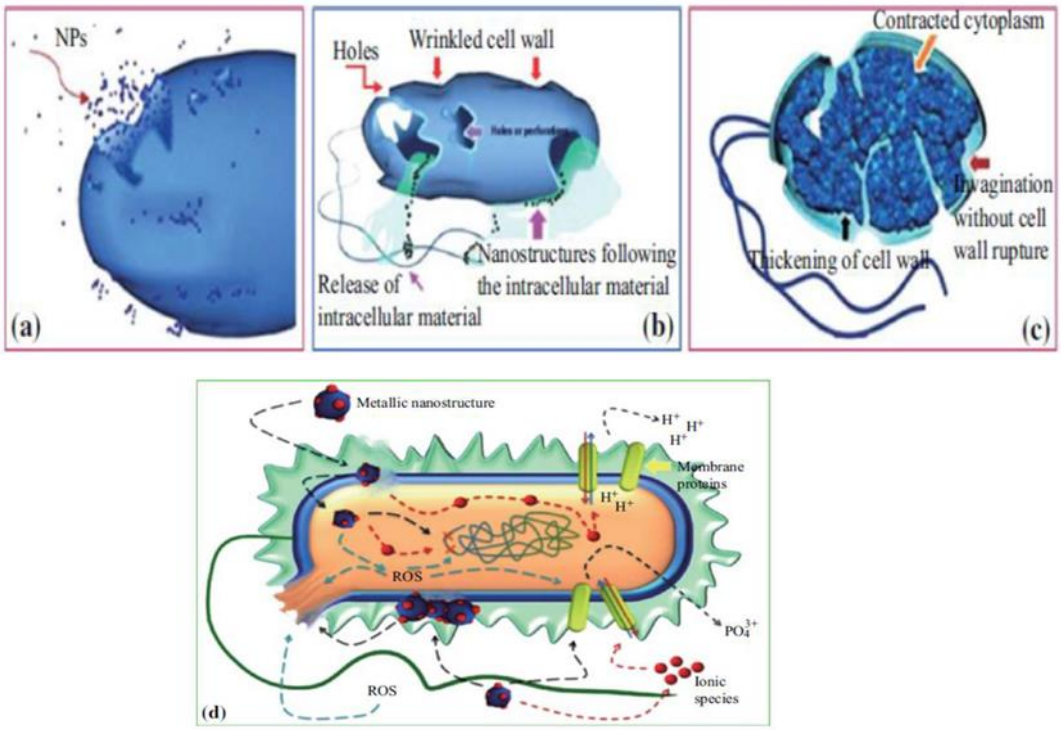
4- Mechanisms of action Nanoparticles

For nanomaterials, most of the antimicrobial resistance mechanisms are insignificant since a nanoparticle's process of action is direct interaction with bacterial cell without the need to penetrate the bacterial cell wall; This gives rise to the hope that NPs will be less likely than antibiotics to induce bacterial resistance. Therefore, interest was focused on exciting and new antibacterial-activity NPs-based materials. In Gram (+) and Gram (-) bacteria, the nanoparticle showed broad-spectrum antibacterial features. Zinc oxide nanoparticles (ZnO

NPs) have been found to growth inhibit *Staph. aureus*, for instance, and silver nanoparticles (AgNPs) tend to be concentration-dependent against *P. aeruginosa* and *E.coli*.

The precise mode of action of nanoparticles has not, however been adequately explained, and contrasting effects are often present in the same types of NPs. Nanoparticles' antibacterial mechanism of action is commonly defined as adhering to 1 of 3 different models: induction of oxidative stress, release of metal ions or mechanisms of non-oxidative [31,32,33].

These three kinds of mechanisms may occur concurrently. Some studies have indicated that silver nanoparticles (AgNPs) cause the neutralization of the bacterial membrane's surface electrical charge and alter its penetrability, eventually leading to bacterial death [34]. In addition, reactive oxygen species (ROS) production inhibits the antioxidant defense mechanism and The cell membrane causes mechanical damage to the membrane. The key processes underlying the antimicrobial effects of nanoparticles are according to current studies, as follows: 1) bacterial cell membrane disruption; 2) ROS generation; 3) membrane penetration into a bacterial cell, and 4) Induce of intracellular antibacterial effects, that including deoxyribonucleic acid (DNA) and protein reactions.



Figure(2): Internalization of NPs into the cell and translocalization

(A) NPs penetrate the cell wall through openings, pits or protrusions. (b) Schematic representation of a collapsed cell demonstrating cell wall destruction and

cytoplasmic material extrusion. (c) Bacterial cells that exhibit major variations in the composition of the envelope (slight invagination and cell wall thickening) and cytoplasm extrusion. (D) Possible mechanisms include the absorption of metal ions inside cells, intracellular permeability and DNA replication destruction, the release of metal ions and the formation of ROS, and the accumulation and decomposition of NPs in the bacterial cell membrane [35].

It has been shown that Ag NPs with diameter of 21 nm an average inhibit different growth of bacterial Gram-negative like Cholera of Vibrio*, E. Coli*, and *P. aeruginosa* and *S. Typhi* when growth on plates of agar with NP concentrations above or below 75 μg/mL[36] The bactericidal effect of Ag NPs was attributed to a variety of mechanisms by the study community. Firstly, it was thought that membrane permeability was effective. The presence within the bacterial cell of a large number of NPs indicates that this is an important mechanism. The microbe membrane and intracellular protein reaction of silver nanoparticle, In specific, membrane proteins containing sulfur and DNA-containing phosphorus, interaction with division of cell that lead to cell death.

In one analysis, the ZnO nanoparticle was tested on various bacterial species and all bacterial species were found to be more toxic than other comparable particles. The mechanism of the ZnO nanoparticle's antimicrobial efficiency is complex and not completely understood. Zn ions are known always to inhibit various activities such as transmembrane proton translocation, glycolysis, and acid tolerance in the microbial cell [37].

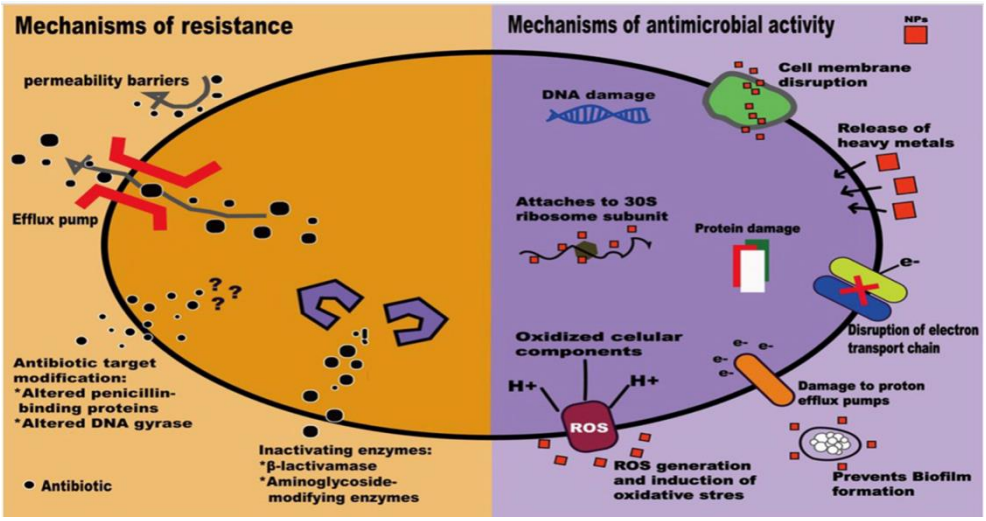
In another study, iron oxide NPs with diameter (9 nm) as in average and length of (100–200 nm) was shown to inhibit *Staphylococcus aureus* viability, as shown by a decline in the live cell to dead cell ratio. Iron oxide NPs were shown to decrease cells viability in (4, 12, 24) hrs. at concentrations of (3 mg/mL) relative to bacterial culture controls without nanoparticles and lower nanoparticle concentrations. It was thought that the antibacterial events of iron oxide NPs was related to the ability of NPs to enter the bacterial cell and produce reactive O2 species [38].

5- Nanotechnology-Applications in Antibacterial Therapies

In order to avoid the disastrous effects of antibiotic resistance, antimicrobial applications of nanotechnology are gaining momentum. It is possible to use nanomaterials to prepare preventive therapies, diagnostics and drug carriers. Compared to their bulk form, nanomaterials have specific features that render them ideal for antibacterial therapies.

Several nanoparticles (NPs) connote antibacterial activities that are not known in their bulk type. With NPs-based approaches, fast and responsive microbial detection can be given.

As antimicrobial drug delivery systems, NPs also provide distinct benefits and can be intended as combinatorial delivery systems, environmentally responsive, targeted [39]. A vaccine that includes NPs as adjuvants or delivery vectors that cause immune system responses against infection of bacterial is another strategy for nanomaterials as antibacterial treatment[40]. Extreme infections are a common cause in health facilities and the environment. Its resistance to the antibiotic methicillin [41].



Mechanisms of antimicrobial resistance [42] and actions of nanoparticles [43]

Metal NPs have been modified for immunization, infection detection and treatment and cross infection control applications[44]. There are several advantages conferred by the use of these NPs-based systems, namely: I enhancing the rate and efficiency of drug absorption by epithelial diffusion; (ii) preventing the drug from degrading during its transfer to the target tissues; and (iii) Enhancement of intracellular penetration quality and subsequent distribution. In addition, the broad surface-to-volume ratio of these NPs, whether a particular biological molecule or a microbial cell, permits greater contact with the surface of the target molecule. Their comparatively small size often allows certain kinds of biological membranes such as blood to be bypassed, a brain barrier that can not be reached by traditional therapeutic methods [45].

Nanoparticles (NPs) used in drug delivery have been documented in several studies, including liposomal NPs, polymer-based NPs, solid lipid NPs, and terpenoid-based NPs. As inorganic nanodrug carriers, mesoporous Silica NPs, magnetic NPs, carbon NPs and quantum dots have promise. The small sizes of the NPs make them ideal to combat intracellular bacteria for antibacterial purposes [46]. With a view to increasing bioavailability, because of their structure and compatibility with biological constituents, antibacterials have been coupled with liposomes or NPs. With a view to increasing bioavailability, because of their structure

and compatibility with biological constituents, antibacterials have been coupled with liposomes or NPs. Colloidal particles, which are biodegradable polymers, play an important role in potential antimicrobial chemotherapy applications. However, due to their polymeric nature, NPs in biological fluids tend to be more stable than liposomes. Different studies have recently focused on the delivery of antibiotics via liposomes or nanoparticles [47].

Conclusion:

It should be considered that several aspects are mainly taken into account when using nanomaterials as antimicrobial agents. Due to the long production-consumption period, antibacterial resistance to popular chemical antibacterial substances may reduce their efficiency and the use of low quality or fake drugs in undevelope and developing countries. As an antimicrobial substanc, NPs have become the latest solution to this problem, which can provide an efficient nanostructure to deliver the antimicrobial substances effectively to target the bacterial community; they are also so potent that microbial pathogens can not resist them. On the other hand, at successful concentrations used to destroy bacterial cells, most of the metal oxides NPs have little toxicity against humans, which thus becomes a benefit for full-scale use. Over the current decade, however, numerous reports have indicated that NPs are very good antibacterial substances, at least at the level of science.

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