Nanotechnology Strategy as Antibacterial: a Primer for the Notice.

Tope Abraham Ibisanmi (Topeibisanmi@gmail.com)
Federal University of Technology Akure https://orcid.org/0000-0002-5540-0795

Research Article

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Abstract

Background: Multidrug-resistant (MDR) bacteria pose a major threat to all fields of medical science as it can result in treatment failure which can have severe consequences, especially in case of critical patients. The availability of new antibacterial agents appeared to be a very complex process. Nanotechnology is an important field of modern research dealing with design, synthesis, and manipulation of particle structures ranging from approximately 1-100 nm.

Main body: Nanoparticles (NPs) have wide range of applications in areas such as health care, cosmetics, food and feed, environmental health e.t.c. Nanosystems can be categorized based on their matrix properties and the material constituting them into inorganic and organic nanosystems. Techniques use in the synthesis of NPs includes; chemical, physical, photochemical, and biological methods. Each method has its pros and cons with common problems of cost, scalability and uniform particle size. Famous microbiologist Alexander Fleming said that “There is probably no chemotherapeutic drug to which in suitable circumstances the bacteria can not react by in some way acquiring fastness.” Therefore, there is high probability that the organism may also become resistance to newly developed drugs at later stage, further these drugs are highly expensive.

Conclusion: To this end NPs are considered to be good antibacterial agents and may overcome the barrier of MDR owing to their multifunctional mechanisms to intervene normal cell functionality, ability to anchor to the bacterial cell wall and subsequently penetrate it, thereby causing structural changes in the cell membrane permeability leading to cell death.

1. Background

Multidrug-resistant (MDR) bacteria pose a major threat to all fields of medical science as it can result in treatment failure which can have severe consequences, especially in case of critical patients [1]. At present some of the most challenging Multidrug-resistant (MDR) organisms are extensively drug-resistant (XDR) *Mycobacterium tuberculosis*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus* (MRSA), *Escherichia coli* and *Klebsiella pneumonia* and so on [2]. The availability of new antibacterial agents appeared to be a very complex process in view of the capability to produce new effective and safe drugs, in addition to the high production costs and the time required for approval of new drugs that takes about 10–15 years [3].

Nanoparticles are particles between 1 and 100 nanometres (nm) in size with a surrounding interfacial layer. The interfacial layer is an integral part of nanoscale matter, fundamentally affecting all of its properties [4]. The interfacial layer typically consists of ions, inorganic and organic molecules. Organic molecules coating inorganic nanoparticles are known as stabilizers, capping and surface ligands, or passivating agents [4].

Nanomedicine plays a vital role in enhancing the effectiveness of existent therapeutics, by enhancing the physicochemical properties and stability of antibiotics, offering a chance of biofilm internalization,

prolongation of antibiotic release, in addition to the capability of targeted delivery to the site of infection and improved systemic circulation with a consequent reduction of the related side effects compared to the corresponding free drugs [5].

2. Main Text

2.1 Nanoparticles

Nanotechnology is an important field of modern research dealing with design, synthesis, and manipulation of particle structures ranging from approximately 1-100 nm. Nanoparticles (NPs) have wide range of applications in areas such as health care, cosmetics, food and feed, environmental health, mechanics, optics, biomedical sciences, chemical industries, electronics, space industries, drug-gene delivery, energy science, optoelectronics, catalysis, single electron transistors, light emitters, nonlinear optical devices, and photo-electrochemical applications.

Nanoparticles can be made of materials of different chemical nature such as metals, metal oxides, silicates, non-oxide ceramics, polymers, organics, carbon and biomolecules. Nanoparticles also exist in several different morphologies such as spheres, cylinders, platelets and tubes [6].

Nano particles can be broadly grouped into two, namely, organic nanoparticles which include carbon nano particles (fullerenes) and the inorganic nanoparticles which include magnetic nano particles, noble metal nano particles (gold and silver) and Semi-conductor nano particles (titanium oxide and Zinc oxide) [5] Nano materials have unique physicochemical and biological properties as compared to their larger counterparts [7]. The properties of nano materials can greatly influence their interactions with bio molecules and cells, due to their peculiar size, shape, chemical composition, surface structure, charge, solubility and agglomeration. For example, nano particles can be used to produce exceptional images of tumor sites; single-walled carbon nanotubes, have been used as high-efficiency delivery transporters for biomolecules into cells [8]. By further research in nanotechnology, it can be useful for every aspect of human life such medicine, regenerative medicine, stem cell research and nutraceuticals are among the leading sectors that will be modified by nanotechnology innovations. Silver NPs are of interest because of the unique properties (e.g. size and shape depending optical, electrical, and magnetic properties) which can be incorporated into antimicrobial applications, biosensor materials, composite fibers, cryogenic superconducting materials, cosmetics products, and electronic components [9]. It is also useful when incorporated into antimicrobial applications, biosensor materials, composite fibers, cryogenic super-conducting materials, cosmetic products, and electronic components. Some important applications of silver NPs are in pharmaceutics, medicine, and dentistry e.t.c. Several physical and chemical methods have been used for synthesizing and stabilizing silver nanoparticles [10].

2.2 Classification of Nanosystems

Nanosystems can be categorized based on their matrix properties and the material constituting them into inorganic and organic nanosystems [11]. Inorganic nanosystems represent a class of nanosystems that originates from inorganic oxides. Their synthesis technique depends on chemical reduction of metallic salts with a reductant. The reaction environmental parameters, for example temperature and pH, play a major function in determining the specificities of these materials, consequently affecting their loading capacity, the in vitro drug release kinetics, aggregation, and hence their antibacterial affect [12]. Furthermore, organic nanosystems such as liposomes, lipid-based nanoparticles, polymeric micelles and polymeric nanoparticles have preferable biodegradability and biocompatibility features, making them suitable candidates for clinical use [13].

2.2.1. Organic Nanosystems

2.2.1.2 Liposomes _ Composition and Characteristics of Liposomes

Liposomes are considered the most extensively evaluated antimicrobial drug delivery nanosystems. They are characterized by spherical structures made up of phospholipid bilayer(s) surrounding an inner aqueous space, ranging in size from 0.02 to 10nm. The efficacy of antibacterial-loaded liposomes in biofilm eradication relies on the physicochemical properties of liposomes that control their stability and in vivo interactions. For antibiotic delivery small unilamellar vesicles of '100 nm displayed high capability in the eradication of bacterial strains. Liposomes proved to be useful for the management of topical, vaginal, pulmonary, and ocular bacterial infections [14].

2.2.1.2.3 Advantages of Antibiotics-Loaded Liposomes as Drug Delivery Agents

- Better protection and enhanced antibiotics biodistribution.
- Selective biofilm targeting affinity.
- Improved selectivity towards intracellular and extracellular bacterial strains.

2.2.2 Bimetallic NPS

Ag and Au may be used in a single NP to enhance the effects of a drug and reduce the required dose. Alternatively, they can be used alone since they possess antimicrobial properties that are enhanced when combined in the form of bimetallic NPs [4]. The role of Ag against MDR pathogens has been previously described. AuNPs constitute good vectors to the delivery of pharmacologic compounds. Gold(Au)-silver(Ag) alloys are an optimal solution since they combine the antimicrobial effect of silver with the

ease of functionalization and improved stability in complex biological media provided by gold. Fakhri and co-workers synthetized and functionalized AgAuNPs with a tetracycline and concluded that there exists a synergetic effect of the antibiotic with the bimetallic nanoparticle, with greater bactericidal activity of this form in detriment of its free forms [15].

2.2.2.1 Silver Nanoparticles (AGNPS)

Since the ancient times, silver has been recognized as having antimicrobial effects [16]. Based on all the evidence to date, AgNPs are probably one of the most promising inorganic NPs that can be used for the treatment of bacterial infections [5]. These NPs may be synthesized by traditional chemical reduction or via “green” chemistry approaches using plant and/or microbial extracts [17]. Several mechanisms have been proposed to understand how AgNPs mediate cell death, including cell wall disruption [15], oxidation of cellular components, inactivation of the respiratory chain enzymes, production of ROS, and decomposition of the cellular components. The permeability of the membrane increases after incorporation of AgNPs into the cell membrane. The adsorption of the NPs leads to the depolarization of the cell wall, altering the negative charge of the cell wall to become more permeable. It was demonstrated disruption of the cell wall with subsequent penetration of the NPs. The entry of AgNPs induces ROS that will inhibit ATP production and DNA replication. However, there is evidence that AgNPs can release Ag+, known to exhibit antimicrobial activity, when interacting with thiol-containing proteins, which weaken their functions. The precise method of the antibacterial mechanism of AgNPs is still not completely understood [15]. All the existing data indicates that AgNPs exert several bactericidal mechanisms in parallel, which may explain why bacterial resistance to silver is rare. Concerns regarding the cytotoxicity and genotoxicity of AgNPs have been raised but various authors have conducted clinical trials based on AgNPs and no important clinical alterations have been detected. Interestingly, AgNPs have been found to exhibit higher antimicrobial activity than antibiotics like gentamicin or vancomycin against P. aeruginosa and MRSA [17].

2.2.2.2 Gold Nanoparticles (AuNPs)

Metallic gold is considered inert and non-toxic, which may vary when it shifts form metallic bulk to oxidation states (I and II). Gold NPs (AuNPs) may be synthesized by traditional chemical reduction of a gold salt or via “green” chemistry approaches using plant and/or microbial extracts. naopartices of an alloy of gold have yellow colour (Fig. 1). The most used and described method is the chemical synthesis based on the reduction of chloroauric acid by citrate [18]. Some studies have addressed the potential of using AuNPs as antibacterial agents, but some controversy still exists. According to Yu H and collaborators, AuNPs are usually not bactericidal at low concentrations and weakly bactericidal at high concentrations. This is possibly due to the effect of co-existing chemicals, such as gold ions, surface coating agents, and chemicals involved in the synthesis that were not completely removed. the antibacterial mechanism of AuNPs is associated to (i) the collapse in the membrane potential, hindering

ATPase activity causing a deterioration of the cell metabolism; (ii) hindering of the binding subunit of the ribosome to tRNA ; and (iii) Shamaila and co-workers showed that AuNPs may affect the bacterial respiratory chain by attacking nicotinamide [15].

2.2.2.3 Metal Oxides

Metal oxides NPs are among one of the most explored and studied family of NPs and are known to effectively inhibit the growth of a wide range of sensitive and resistant Grampositive and -negative bacteria, emerging as hopeful candidates to challenge antimicrobial resistance [19]. Iron oxide (Fe3O4), Zinc oxide (ZnO), and Copper oxide (CuO) possess antimicrobial properties and can be applied in clinical care. Due to the intrinsic photocatalytic activity of the metal oxides they generate ROS and become powerful agents against bacteria These will be described in more detail on the following sections [15].

2.2.2.4 Iron Oxide (FE3O4)

The synthesis of iron oxide NPs may be achieved via different routes. The antibacterial mechanism of these NPs is mainly attributed to dissolved metal ions and the generation of ROS [1]. It was shown that superparamagnetic iron oxide NPs interact with microbial cells by penetrating the membrane and interfering with the electron. Additionally, it has been described that iron oxide NPs can damage macromolecules, including DNA and proteins, through the formation of ROS.

2.3 Synthesis Methods of Nanoparticles

Synthesis Methods of Silver Nanoparticles

Many techniques have been used for the synthesis of Ag-NPs by using chemical, physical, photochemical, and biological methods (Fig. 2). Each method has its pros and cons with common problems of cost, scalability, uniform particle size, and the size distribution [2]. Traditionally, metal nanoparticles are produced by physical methods like ion sputtering or pulsed laser ablation and chemical methods such as reduction, thermal synthesis, hydrothermal, sol-gel methods, and so on. However, recently, the environmentally friendly synthesis methods (by using natural products) have been developed under the branch of “green syntheses.” Depending upon the selected path of synthesis and different experimental conditions, the silver NPs of different morphology, sizes, and shapes can be obtained. Nevertheless, the most important criteria is the size distribution that should be achieved as narrow as possible for the target-specific applications. Four important methods (chemical, physical, photochemical, and biological) for the synthesis of nanoparticles are discussed as follows [2].

2.3.1 Chemical method of synthesis

Among the existing methods, the chemical methods have been most common used for the production of Ag-NPs. The chemical reduction of metal ions is the most universal and easy route for the preparation of the metal nanoparticles [20]. The chemical transformation of the silver ions into the silver nanostructures can occur using photochemical method, wet chemical synthesis with or without templates, by employing liquid crystal, polymer templates, solution-based methodologies such as aspartate reduction and starch-mediated reduction, etc. Generally, the chemical synthesis process of the Ag-NPs in solution usually employs three main components which includes metal precursors (for formation of AgNPs: AgNO 3 AgClO 4, AgCl, (PPh 3) 3AgNO 3, CF3CooAg), reducing agents and stabilizing/capping [21].

2.3.2 Physical method of synthesis

In the physical synthesis process of Ag-NPs, usually, the physical energies (thermal, ac power, and arc discharge) are utilized to produce Ag-NPs with a narrow size particle distribution. This approach can permit us to produce large quantities of Ag-NPs samples in a single process [20].Under the physical methods, the metallic NPs can be generally fabricated by evaporation-condensation process that could be carried out in a tube furnace at atmospheric pressure. The large space of tube furnace, consumption of large amount of energy, raising the environmental temperature around the source material and a lot of time for achieving thermal stability, these are among the few drawbacks of the method. Another physical method of synthesis of Ag-NPs is a thermal decomposition method that used to synthesize the powdered Ag-NPs. This indicates that the Ag-NPs were prepared with a very narrow size distribution for synthesizing the metal NPs and by evaporating the source materials under the flow of carrier gas, i.e., air. It had been reported that the geometric mean diameter, the geometric standard deviation, and the total concentration of spherical NPs without agglomeration increases with the temperature of the surface of the heater [20].

2.3.3 Photochemical synthesis of nanoparticles

The photo-induced synthesis of Ag-NPs has two main approaches. In top down method, NPs could be prepared by the fragmentation of the bulk metals and followed by generation of the NPs from ionic precursors [20].The NPs are formed by the direct photoreduction of a metal ion using photo-chemically generated intermediates, such as excited molecules and radicals, which are often known as photosensitization of NPs. The main advantages of the photo-induced process are: clean process, high spatial resolution, convenience of use, the controllable in-situ reducing agents generation. The photo-induced silver nanoprisms/nanodecahedrons have been the synthesis by controlling the concentration of sodium citrate and sunlight (ultraviolet light). At the lower concentration of citrate ($\leqslant 5.0 \times 10^{-4}$ M), silver nanoprisms are converted into nanodecahedrons silver by increasing the concentration of citrate. Although the intensity of light affects the shape of the NPs, the lighting power density did not influence the shape conversion except for reaction rate [16].

2.3.4 Biological synthesis of nanoparticles

Usually, wet-chemical or physical method is used to prepare the metal nanoparticles. However, the chemicals used in physical and chemical methods are generally expensive, harmful and inflammable but the biogenic methods are a cost effective, energy saver and having environmentally benign protocols technique for green synthesis of silver nanoparticles from different microorganisms (yeast, fungi and bacteria, etc.) and plant tissues (leaves, fruit, latex, peel, flower, root, stem, etc.) [20]. Pytochemicals (lipids, proteins, polyphenols, carboxylic acids, saponins, aminoacids, polysachccarides amino cellulose, enzymes, etc.) present in plants are used as reducing and capping agent. The use of agro waste and microorganisms materials not only reduces the cost of synthesis but also minimizes the need of using hazardous chemicals and stimulates green synthesis.

This method of biosynthesis is very simple, requiring less time and energy in comparison to the physical and chemical methods with predictable mechanisms. The other advantages of biological methods are the availability of a vast array of biological resources, a decreased time requirement, high density, stability, and the ready-to-soluble as-prepared nanoparticles in water. Therefore, biogenic synthesis of metal NPs unwraps up enormous opportunities for the use of biodegradable or waste materials.

2.3.4.1 Biosynthesis of silver nanoparticles using bacteria

Bacterial cells possess a special mechanism of resistance of silver ions in the environment; this innate feature is responsible for growth and survival in the environment with metal ion concentration and their ability to synthesize nanoparticles. The mechanism involved in the resistance are efflux system alteration of solubility and toxicity via reduction or oxidation, absorption, bioaccumulation, extracellular complex formation or precipitation of metals and lack of specific metal transport system (Thu *et al.,* 2013).

Several bacteria have been documented to synthesize silver nanoparticles. Silver nanoparticles at 440 nm peak which corresponded to the surface plasmon resonance of silver nanoparticle were used to extracellularly synthesize silver nanoparticles from nitrate solutions using B. cereus. Furthermore, *Staphylococcus aureus*, Bacillus subtilis, E. coli, P. syringae and Streptococcus species have been reported to produce silver nanoparticle [9].

2.4 MULTIDRUG RESISTANCE (MDR) AND NANOPARTICLES

Multidrug-resistant (MDR) bacteria pose a major threat to all fields of medical science as it can result in treatment failure which can have severe consequences, especially in case of critical patients [1]. At present some of the most challenging Multidrug-resistant (MDR) organisms are extensively drug-resistant (XDR) *Mycobacterium tuberculosis*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus* (MRSA), *Escherichia coli* and *Klebsiella pneumonia* bearing NDM-1 (New Delhi metallo-beta-lactamase-1), vancomycin resistant enterococci (VRE) and vancomycinresistant MRSA. Bacterial antibiotic resistance exhibited by different micro-organisms could be attained through

various intrinsic or acquired mechanism [16]. Intrinsic or ‘natural’ resistance is inherent to a bacterial species and involves the absence of the target or the presence of low-affinity targets, low cell permeability, inactivation of the antibiotics and the presence of efflux mechanisms. On the other hand, acquired mechanisms include mutations in genes targeted by the antibiotics, the transfer of resistance determinants borne on plasmids, bacteriophages, transposons, and other mobile genetic materials. In general, this exchange is accomplished through the processes of transduction (via bacteriophages), conjugation (via plasmids and conjugative transposons), and transformation (via incorporation into the chromosome of chromosomal DNA, plasmids, and other DNAs from dying organisms). A very few novel antibiotics have been discovered to treat these MDR organisms in past decades. Famous microbiologist Alexander Fleming said that “There is probably no chemotherapeutic drug to which in suitable circumstances the bacteria can not react by in some way acquiring fastness.” Therefore there is high probability that the organism may also become resistance to newly developed drugs at later stage, further these drugs are highly expensive. To this end nanoparticles are considered to be good antibacterial agents and may overcome the barrier of MDR owing to their multifunctional mechanisms to intervene normal cell functionality. Nanoparticles are shown to have the ability to anchor to the bacterial cell wall and subsequently penetrate it, thereby causing structural changes in the cell membrane permeability leading to cell death. Silver NPs (SNPs) show efficient antimicrobial property compared with other salts due to their extremely large surface area, which provides better contact with microorganisms. SNPs may target at the bacterial membrane, leading to a dissipation of the proton motive force which in turn cause blocking of oxidative phosphorylation.32 Another mechanism involved in microbicidal activity is the generation of free radicals by the nanoparticles which have the ability to damage the cell membrane and make it porous which can ultimately lead to cell death. Metal nanoparticles have the affinity to interact with sulfur and phosphorus containing biomaterials present in the bacterial cell e.g., DNA bases. The metal nanoparticles can act on these soft bases and destroy the DNA which would lead to cell death. Nanoparticles are known to modulate the bacterial signal transduction [4]. The nanoparticles dephosphorylate the peptide substrates on tyrosine residues, which lead to signal transduction inhibition and inhibition of bacterial growth. It is also shown that there could be a release of silver ions from Ag nanoparticles and these ions can interact with the thiol groups of many vital enzymes and inactivate them, causing disruption of cellular functions. NPs also exert their antibacterial activities either by collapsing the membrane potential and inhibiting the ATPase activities to decrease the ATP level and the other is by inhibiting the subunit of ribosome from binding to tRNA. Several findings on bactericidal effect of various NPs and nanoconjugate systems are briefly reviewed in preceding sections [2].

2.5 NANOSYSTEMS’ ROLE IN OVERCOMING ANTIBIOTIC RESISTANCE

The emergence of aggressive bacteria together with the limited production of new antibacterial drugs has resulted in inefficiency of current antibiotic therapy with relevant risks on human health. The availability of new antibacterial agents appeared to be a very complex process in view of the capability to produce

new effective and safe drugs, in addition to the high production costs and the time required for approval of new drugs that takes about 10–15 years [4,5]. In 2016, many antibiotics were clinically tested for the market in the United States of America [2]. Sadly, however, in the last decades, linezolid was the only approved antibiotic together with the recently discovered teixobactin (Nermin *etal.,* 2020. Nanomedicine plays a vital role in enhancing the effectiveness of existent therapeutics, by enhancing the physicochemical properties and stability of antibiotics, offering a chance of biofilm internalization, prolongation of antibiotic release (Fig. 3), in addition to the capability of targeted delivery to the site of infection and improved systemic circulation with a consequent reduction of the related side effects compared to the corresponding free drugs [5] .

2.5 Some Nanoparticles and their Bactericidals Action

2.5.1 Silver Nanoparticles

Among metal nanoparticles silver nanoparticles have been extensively studied and used as effective antimicrobial agents. The bactericidal effect of silver nanoparticles on micro-organisms is very well known; however, the bactericidal mechanism is not completely understood. Studies showed that silver nanoparticles attacks Gram negative bacteria by anchoring and penetrating the cell wall, and as a consequence, the leading structural change in the membrane morphology. This result in significant increase in membrane permeability and alters transport through the plasma membrane resulting in cell death [4]. It has also been proposed that the silver nanoparticles strongly interact with thiol groups of vital enzymes and phosphorus-containing

2.5.1.1 Action of Silver Nanoparticle on Microbes

There are various theories on the action of silver nanoparticles on microbes to cause the microbiocidal effect. Silver nanoparticles have the ability to anchor on the bacterial cell wall and subsequently penetrate it, thereby causing structural changes on the cell membrane like permeability of the cell membrane and death of the microbial cell. There is formation of peats on the cell surface as well as accumulation of nanoparticles on the cell surface (Fig. 4). The formation of free radicals on the microbial cell surface by the silver nanoparticles maybe considered as another mechanism by which death of the microbial cell may occur [6].

2.5.2 No Releasing Nanoparticles

Besides silver nanoparticles, nitric-oxide-releasing NPs (NO NPs) also possess broad spectrum antibacterial activity which can inhibit the growth of many antibioticresistant and sensitive bacteria such

as K. pneumoniae, E. faecalis, S. pyogenes, E. coli, and P. aeruginosa. NO is a lipophilic and hydrophilic natural gas, and is unstable in an oxygen environment. Reactions of NO with oxygen or superoxide spontaneously produce reactive nitrogen and oxygen intermediates that are toxic to the cell and act as antimicrobial species [4].

2.5.3 Dinitrogen Trioxide and Dinitrosyl-Iron

complexes are generated. NO-associated lipid damage has been demonstrated with peroxynitrite and nitrogen dioxide. Peroxynitrite mediate lipid peroxidation of liposomes which contribute to the antimicrobial activities of NO [22]. NO interactions with proteins involve reactive thiols, heme groups, iron-sulfur clusters, phenolic or aromatic amino acid residues, tyrosyl radicals, or amines [14]. Peroxynitrite and NO•2 also nonspecifically oxidize proteins at a variety of sites.73 Studies of NO-related cytotoxicity have demonstrated inactivation of enzymes containing Fe-S clusters (e.g., aconitase, NADH dehydrogenase, succinate dehydrogenase) suggesting that NO• (NO radical) might directly release iron from metalloenzymes and cause iron depletion.74 RNOS also causes DNA damage through autoxidation of NO where N-nitrosating intermediates deaminate cytosine, adenine and guanine. The antimicrobial and healing efficacy of sustained release nitric oxide nanoparticles have been investigated against methicillin-resistant SA (MRSA) and *Acinetobacter baumannii* using a murine wound and soft [4].

2.5.3 Metal Oxide Nanoparticles

Metal oxides nanoparticles (NPs) such as TiO2, CuO and ZnO are known to exhibit good antibacterial properties [23]. One of the common properties they share is their photocatalytic activity due to wide band gap. The photocatalytic activity is attributed to generation of reactive oxygen species (ROS). Copper (CuO) nanoparticles have shown activity against a range of bacterial pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA) and *Escherichia coli*, Furthermore, the ability of CuO nanoparticles to reduce bacterial populations to zero was found to be enhanced in the presence of silver nanoparticles [19].

3. Conclusions

The wide spread antibiotic resistance has put immense pressure on pharmaceutical industries to search new antimicrobial agents or modification of the existing drugs. In an area such as MDR, nanotechnology has potential to change the scenario and prevent the spread of drug resistance. Metallic nanoparticles of both biological and chemical origin are shown to be potential agents in antibacterial treatment. Nanoparticles not only demonstrated activity against MDR bacteria themselves, but also showed potential for the development of synergistic combinations that increases the antibacterial effect of existing antibiotics. They helped to revive the antibacterial activity of old generation antibiotics against which microbes have developed resistance. The review showcased the effect of various forms of radiations in combination with nanoparticles enhancing the antibacterial efficacy. Further work is still

required in order to elucidate the entire mechanism of action of nanoparticles as bactericidal, toxicity of nanoparticles in human and better delivery of drug inside human system using nanodrug carriers. Nanoparticles coupled with either antibiotics and/or irradiation may provide a potential strategic remedy to combat MDR.

Further work is still required in order to elucidate the entire mechanism of action of nanoparticles as bactericidal, toxicity of nanoparticles in human and better delivery of drug inside human system using nanodrug carriers. Therefore, scientists should carry out more research on this field,

Abbreviations

MDR: Multidrug-resistant, XDR: extensively drug-resistant, NPs: Nanoparticles, MRSA: methicillin-resistant *Staphylococcus aureus*, ROS: reactive oxygen species, DNA: Deoxyribonucleic acid, VRE: vancomycin resistant enterococci, SNPs: Silver nanoparticles, ATP: Adenosine triphosphate

Declarations

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Authors' contribution

The study was collectively executed by all authors. TAI: conceived and prepared the manuscript. JOA: substantial contributions to the conception. All authors read and approved the final manuscript.

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Availability of data and materials

The authors declare that the data supporting the findings of this study are available within the article.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interest

The author declare that he has no competing interest.

Authors' information

[1]Department of Microbiology, School of Sciences, Federal University of Technology, P.M.B. 604, Akure, Ondo state, Nigeria.

[2]Department of Microbiology, School of Sciences, Federal University of Technology, P.M.B. 604, Akure, Ondo state, Nigeria.

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Figures

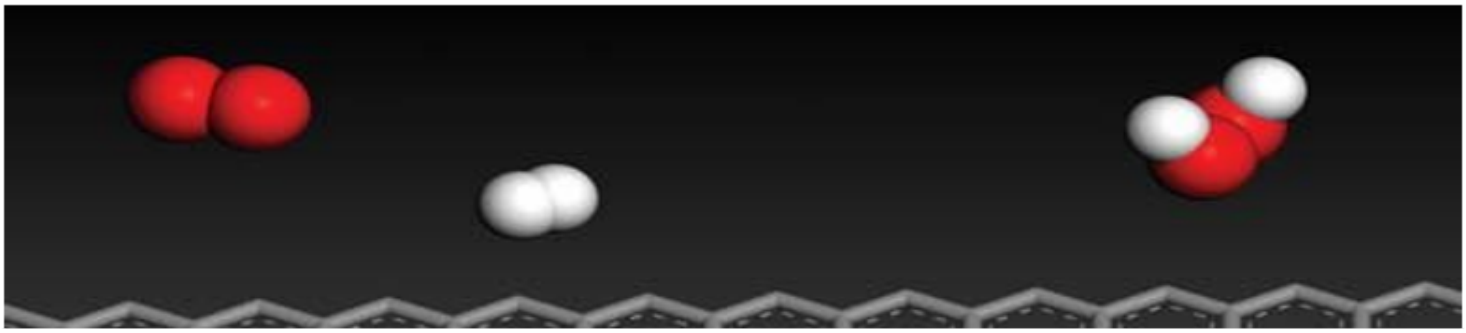

Figure 1

image showing naopartices of an alloy of gold (yellow) and palladium (blue)

Figure 2

Methods for synthesis of Nanoparticles

Figure 3

Graphical outline of various classes of nanosystems with illustration of their possible anti-biofilm mechanisms

Figure 4

Silver nanoparticles destroyed bacteria cell