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NANO-BIOTECHNOLOGY AS FRONTIER IN TRACKING ANTIMICROBIAL RESISTANCE: MECHANISMS AND APPLICATIONS

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Abstract
Antimicrobial resistance (AMR) pretenses a critical universal wellbeing hazard, demanding advanced strategies to battle drug-resistant pathogens. Nano-biotechnology, a cross-disciplinary field at the juncture of nanotechnology and biomedicine, has arisen as an auspicious opportunity for addressing this task. This abstract offers a brief impression of the role of nano-biotechnology in the battle against AMR. Nano-biotechnology controls nanomaterials and nanostructures to project new approaches for overpowering resistance mechanisms. By augmenting the effectiveness of current antimicrobial agents, nanomaterials offer a probable solution to the confines of conservative treatments. Moreover, nanocarriers empower targeted and controlled drug delivery, refining therapeutic results while minimalizing adverse effects. In addition to enhancing treatment strategies, nano-biotechnology eases the improvement of innovative diagnostics and monitoring tools. Nano-based biosensors and imaging practices enable prompt and delicate detection of drug-resistant strains, allowing for quick intervention and particular management of infections. While the potential profits are substantial, trials such as biocompatibility, noxiousness, and ethical contemplations must be addressed for accountable and safe enactment. Interdisciplinary association among investigators, healthcare professionals, and policymakers is critical to translating these progressions into practical solutions. This abstract highlight the noteworthy promise of nano-biotechnology in the constant battle against AMR, accentuating its potential to transfigure the field of infectious disease management and contribute to worldwide public health efforts.
Keywords: *Antimicrobial resistance, nanomaterials, nanostructures, nanocarriers, drug delivery, diagnostics and monitoring tools, biocompatibility, public health.*

Introduction

AMR among hazardous bacteria has unexpectedly increased, posing a major hazard to human well-being. Antibiotics have indisputably facilitated humans to treat a wide range of infectious

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illnesses. In addition to the human population, the agricultural and animal husbandry sectors have long employed antibiotics substantially for therapeutic purposes [1]. Since that antibiotic-resistant bacteria are usually found in animals, the potential harm that these microorganisms might bring to people is a serious public health concern. These bacteria may easily infect humans via the food chain, and they can spread across the environment through animal excrement [2]. The interaction between animals and the environment has a major impact on public health outcomes. Specifically, the soil and aquatic habitations are thought to be vital sources and pools of AMR, particularly as they are influenced by agricultural practices.

Antimicrobial resistance statistics (WHO)

Antimicrobial resistance (AMR) is a serious danger to public well-being and global development. It is estimated that 1.27 million deaths worldwide in 2019 were caused directly by bacterial resistance. The overuse and abuse of drugs in individuals, plants, and animals is the main cause of the rise of drug-resistant diseases. Any country, regardless of geography or economic standing, is affected by AMR; however, middle- and low- income countries are excessively affected, moreover inequality and poverty exacerbate the disease's causes as well as effects. AMR puts many medical breakthroughs at risk, by making infections more problematic to cure and raising the dangers of a variety of medical procedures and therapies, including cancer chemotherapy, cesarean deliveries, and operations. The world has a problem with antibiotic availability and the pipeline for their development, which is made worse by rising antibiotic resistance and a deficiency in scientific research and development. To guarantee fair access to both current and novel vaccinations, tests, and drugs, immediate action is needed. AMR causes significant financial consequences in addition to death and disability. The World Bank estimates that by 2030, AMR may result in annual GDP losses of US$ 3.4 trillion and an added US$ 1 trillion in health care costs by 2050. Antimicrobial resistance (AMR) mitigation in human health necessitates giving top priority to measures including avoiding illnesses that might result in the improper antibiotics use, guaranteeing that everyone has access to top-notch diagnostic and effective infection therapy, and promoting tactical data dissemination and innovation.

Antibiotics and increasing AMR

In the 20th century, several antibiotics were developed to treat bacterial illnesses. As a result of AMR, bacteria adapted to the environment's increasing concentration of antibiotics. An increasing number of AMR infections are presently posing a threat to humanity [3]. Antibiotics act on bacteria by reducing the synthesis of vital proteins, DNA, and RNA and interfering with vital existence methods such the building of cell walls. However, bacteria have the innate capacity to quickly adapt through mutations and transfer of DNA (by horizontal gene transfer), which they have gained during millions of years of competition. Bacteria can also emerge through a variety of ways [4]. Include changes that result in impermeable antimicrobial targets, alterations in acquired genes, enzymatic hydrolysis or destruction, and bacteria dwelling in biofilms [5]

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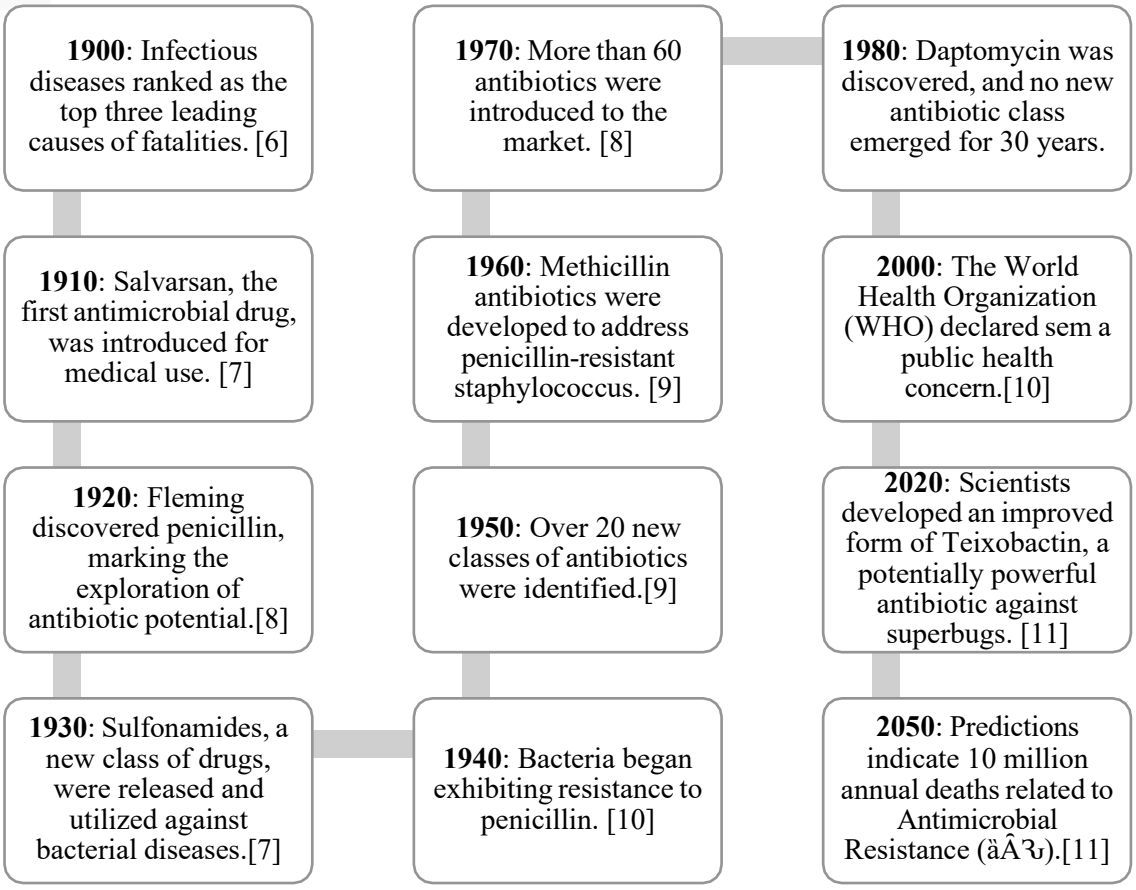

Figure 1: The Antibiotic Development Timeline

Global feat to address antimicrobial resistance

1. **One Health approach**

AMR is a multifaceted issue that calls for coordinated actions from a number of industries, including food production, environmental preservation, animal welfare, and human health. "One Health," a holistic strategy, seeks to sustainably improve human, animal, and ecological health outcomes. This method acknowledges the tight connections and interdependencies that exist amid the health of wild and domesticated animals, plants, and the ecosystem as a whole and the health of humans. Within the context of One Health, initiatives, policies, laws, and research projects are developed, carried out, and overseen cooperatively with stakeholders from pertinent sectors with the goal of preventing and controlling antimicrobial resistance (AMR) and achieving better well-being and financial results.

2. **Antimicrobial Resistance Global Action Plan (GAP)**

The Boards of Directors of the Food & Agricultural Organization of the UN (FAO), the World Organization for Animal Health (WOAH) , and the Environment Program of the UN have accepted the Global Action Plan (GAP) on antimicrobial resistance (AMR). At 2015 World Health Assembly, countries pledged to use a One Health strategy in multisectoral national action plans to tackle antimicrobial resistance (AMR) worldwide.

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3. **Quadripartite Joint Secretariat on AMR**
   The word "quadripartite" mentions to four establishments: UNEP ,WOAH, WHO, and FAO. Quadripartite joint secretariat is hosted by WHO promoting multi-stakeholder contribution in AMR, which has assisted in the creation of several working groups such as the Multi-Stakeholder Partnership Platform (2022) and the Global Leaders Group on AMR (2020). These establishments work meticulously with WHO to synchronize the One Health global response to antimicrobial resistance.
4. **High-level meetings on AMR**
   The UN General Assembly passed a resolution calling for a second High-level Meeting on AMR in March 2022 to be held in 2024, with cooperation of the Quadripartite Organizations and the Global Leaders Group. The AMR Multi-Partner Trust Fund, the Global Action Plan, and groundbreaking multisectoral AMR objectives were also outcomes of three Global High-level Ministerial Conferences on AMR that were held in 2022 in Oman, Europe, and Netherlands. These organizations and co-facilitators are working closely to ensure thoroughgoing participation and inputs from the human, agro-food ,animal and environmental sectors. The high-level meeting represents a significant opportunity for nations to agree on targets and make ambitious commitments.
5. **zzWorld AMR Awareness Week (WAAW)**
   From November 18 to November 24 each year, World AMR Awareness Week (WAAW) in observed worldwide, an official WHO health campaign that aims to raise public awareness, knowledge, and best practices among stakeholders, other policymakers, and the general public. [6].

Categories of nanomaterials

C-Based nanomaterials are NPs that are found as ellipsoids, spheres and hollow tubes because they include carbon. Carbon-based nanomaterials include, fullerenes (C60), graphene (Gr), carbon nanotubes (CNT), carbon black and carbon nanofibers. [12]

1. **Carbon Nanotubes**
   As per studies from 1991, carbon nanotubes (CNTS) are spherical particles connected by covalent connections [13]. The two types of multiwalled (MW) and single-walled (SW) nanotubes are comprised of numerous closely arranged tubes with lengths extending from 100 nm to several micrometers, and various single pipe CNTS with diameters between 1 and 5 nm. In [14] Among carbon-based nanomaterials, SWNTS have demonstrated the strongest antibacterial activity. The first contacts of the SWNTs with bacteria, membrane defects, and membrane oxidation activity that prevents the growth of microorganisms [14] The prospective applications of CNTS in water purification, poliovirus inactivation, *E. Coli* inactivation, and MS2 phage eradication are being continuously studied. [16]
2. **Fullerenes**
   Fullerenes are groups of balls made out of carbon atoms [17]. A number of bacteria against which fullerenes have been demonstrated to exhibit antibacterial activity include *Salmonella*, *Streptococcus* species, and *E. Coli*. Energy is thought to have given them their antibacterial properties. Inhibition of metabolism after nanoparticle uptake by bacteria [18]. An innovative class of synthetic fullerenes was assessed concerning Gram-positive and Gram-negative bacteria, along with their capacity to convey basic or quaternary amino groups. [19]
3. **Inorganic Nanomaterial Silver Nanoparticles (AgNP)**
   Metals such as silver and gold, as well as metallic oxides, may be produced using these nanomaterials. Once antibiotics were discovered in the 1940s, silver's use as an antibacterial

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got limited. Research has demonstrated that the use of AgNP in combination with conventional antibiotics such amoxicillin, vancomycin, and erythromycin increase their collaborative antibacterial activity against both Gram-positive and Gram-negative bacteria along with penicillin G [20]. Later studies found that Ag^{+} ions, which are more likely to bind to nitrogen and sulfur, can connect to amino groups and thiols to inhibit and destroy protein structure. [21]

4. **Gold Nanoparticles**

The manufacture of pharmaceuticals is improved by the use of gold-coated carbon nanotubes. To increase cytometry flow responsiveness, bacteria were colored-changed with gold nanoparticles, which allowed for their identification. The principal mode of action of gold nanoparticles as antibacterial agents is their electrostatic attraction to the bilayer of the cell membrane that is negatively loaded; this notion is additionally supported by the observation that while anionic particles are not harmful, cationic particles may be harmful. [22].When gold Nano cages, nanoparticles, nanorods, and nano shells are exposed to intense laser beams at an appropriate wavelength, they may absorb near-infrared (NIR) radiation, which is commonly used to treat bacterial infections [23]. When it comes to treating serious bacterial infections—especially those brought on by germs that are resistant to many drugs—gold nanoparticles advocate the use of adjuvants rather than antibiotic treatments at lower dosages with less side effects. [24]

5. **Copper Nanoparticles**

Because copper is a basic element of several enzymes produced by microbes, its antibacterial effects are beneficial. Increased Cu2+ ions can produce ROS, which can change the synthesis of amino acids and produce DNA that is more dangerous. [25] Copper microbiological inactivation is based on the "contact-killing" principle. Cu NPs, which have a higher attraction for the carboxyl group and amines on the surface of the bacterium, have demonstrated more efficacy against Bacillus subtilis than silver NPs [26]. Copper oxide (CuO) has poorer overall chemical and physical quality than silver. Reference [27]

6. **Magnesium Oxide Nanoparticle**

One important mechanism behind the antiseptic effect of magnesium oxide (MgO-NPs) is the formation of ROS and other nanoparticles [28]. Consequently, intracellular biomolecules are permanently oxidized by MgO-NPs, leading to the cell's death. Furthermore, numerous studies have revealed that MgO-NPs have a notable degree of antibacterial activity. Research indicates that the release of Mg+2 and ph. Shift are caused by the antibacterial action of MgO-NPs and their adhesion to the microbial cellular membrane [29]. Furthermore, it was demonstrated that halogen molecules sticking to the outside of magnesium oxide was the source of MgO-NPs' antibacterial activity.

Synthesis of nanoparticles

Because of their distinctive qualities, nanomaterials created biologically are more significant than those produced chemically or physically. Nanoparticles can be produced chemically or physically [30]. Many problems, such as the usage of injurious chemicals, the creation of dangerous byproducts, and faults in arithmetic [31]. Particulates from green synthesis may be readily distinguished from physical-chemical particles. The bottom-up strategy for green synthesis is analogous to chemical reduction in that it substitutes natural substance extracts for more expensive chemical-reducing chemicals using fruits or leaves or other living things to produce metals or metal oxides. The nano-particles formed by green synthesis are called "biogenic nanoparticles"[32]. It is simple to separate or up-concentrate drugs when biogenic

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NPs are centrifuged from the reaction media without affecting their biological composition. [33]

1. **Nanoparticles Green Synthesis**

In most cases, the green synthesis will employ either a top-down or bottom-up strategy (Figure 6). A top-down technique including size reduction and several chemical and physical processes is used to manufacture NPs. [34] NPs are made up of smaller structures like molecules and atoms, and their main job in bottom-up synthesis is oxidation/reduction. NPs with reliable chemical properties are extracted using this environmentally benign and sustainable method. In the biological process of creating nanoparticles, plant extracts and microbes are frequently used. [35]

2. **Fungi**

They are vital components of the formation of NPs and active biomolecules that contribute to secondary metabolites. Enzymes, polymers, and proteins produced by fungus such as *Fusarium oxysporum* willingly contribute to the creation of metal nanoparticles. [36]. These elements enhance NP's stability and outcome. Experiments have demonstrated that certain fungal species may create NPs with traces of extracellular amino acids. Most fungus belong to the phytochelatin class, which is very effective in inhibiting silver ions in silver metal. [37] The *Coriolus versicolor* fungus population was used by Sanghi and Verma (2009) to produce silver nanoparticles (Ag NPs). Through the use of FTIR data, the OH- group in fungal mycelium was found in this study. To turn Ag NPs into bare metal, this group adds and subtracts electrons from the silver ion. In fact, verticillium fungus is an eccentric mediator for the synthesis of silver nanoparticles. Intracellular NPs are frequently seen when fungal biomass is treated with agno3 in an acidic medium. [38]

3. **Bacteria**

There are two ways that bacteria make NP: intracellular and extracellular. Extracellular nanoparticles production is more advantageous and takes less time [39]. Dradioduran species have great antioxidant action and are very resistant to radiation as well as oxidative damage. This makes it acceptable to use ionic Au NPs for green synthesis. It has been demonstrated that 2-deoxy guanosine residues and guanine RNA molecules lessen the concentration of gold salt.

4. **Plants**

Numerous biochemicals and metabolites found in plants, including polyphenols, have the ability to serve as stabilizers for production of biogenic NPs. Plants that produce NPs under control fall into three categories: phytochemical, extracellular, and intracellular materials. When starting material is mainly plant extract , the extracellular method is applied. Phytochemical regulated NP synthesis is not a frequently used technology as it demands knowledge of the specific phytochemical essential for balanced NP synthesis. [40]

Characterization of nanoparticles

Wavelengths around 300 and 800 nm are usually used to identify the NPs of around 2 to 100 nm. TEM and SEM provide a description of the morphology and size of NPs. Transmission electron microscopy (TEM) and Scanning electron microscopy (SEM) analyses revealed that the carbon nanotubes comprised entirely of polyaniline layers. XRD examines the sizes, symmetry, and metallic nanoparticle discovery status. Nanoparticles are penetrated by X-rays. The required structural information and the division sequence that was obtained are correlated. At angles of 28.51, 33.06, and 47.42, the XRD peaks (2 hours) of the 111, 200, and 220 planes are situated. The UV—Vis absorption spectrum is used to determine the size and form of NPs

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in an aqueous solution. The NPs, which are between 2 and 100 nm in size, were found using wavelengths between 300 and 800 nm.

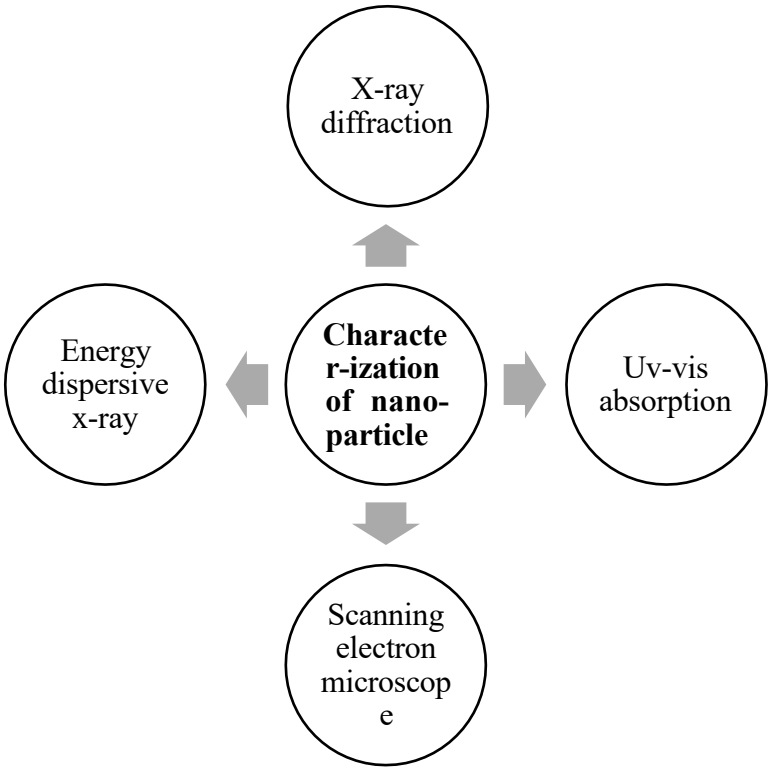

Figure 2. Methods for the characterization of Nanoparticles.

Possible antibacterial & antifungal mechanisms of nano particles

The antimicrobial properties of nanoparticles (NPs) have been accredited to several mechanisms, and while the precise details are not entirely understood, numerous theories have been proposed. One of these theories involves the release of metal ions [41] from nanoparticles, especially when metallic nanoparticles are used, reactive oxygen species-mediated antibacterial activity [42], contact killing [43], combined mechanism [44] and immune system stimulatory effect [45].

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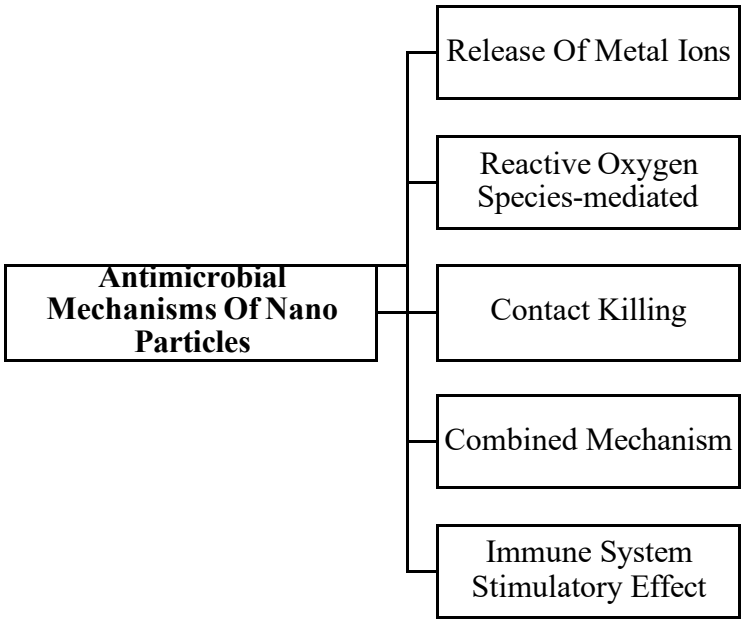

Figure 3: Possible Antimicrobial Mechanisms of Nano Particles

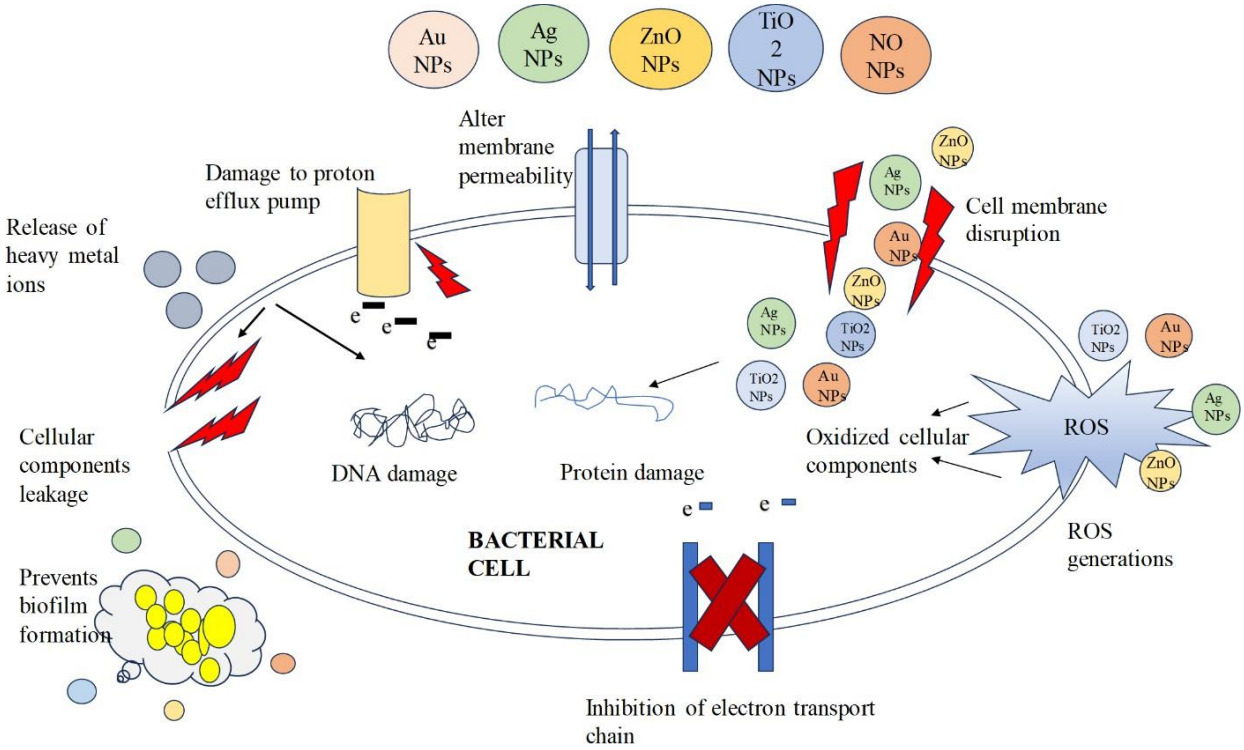

Figure 4: Bacterial Mechanisms of Nanoparticles

1. **Release of Metal Ions**

The antiseptic mechanism of silver nanoparticles (Ag NPs) largely involves the release of silver ions (Ag ions) which interact with bacterial cells [46]. This interaction disrupts membrane

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proteins, affecting membrane permeability and leading to cell death. The process likely involves the interaction of Ag ions with cysteine residues, deactivating crucial proteins within the bacterial cells. This disruption also impacts the transcriptional responses of DNA and RNA within the bacteria. Research has indicated that Ag NPs' antibacterial efficacy is influenced by their surface charge [47]. Ag NPs with a positive charge is more effective against microbes than those with a negative charge. This is explained by the electrostatic contact that occurs amongst the negatively charged cell walls of bacteria and the positively charged nanoparticles [48]. Stronger antibacterial activity and easier bacterial contact are made possible by a reduced electrostatic barrier caused by NPs with higher positive surface charges [49]. Furthermore, studies have been done in which Ag NPs were enmeshed in a matrix that just permitted the formation and release of ions, therefore isolating the effects of the NPs themselves [50]. This work confirmed that the antibacterial qualities of silver NPs are typically due to the released ions, underscoring the key function of ions in antimicrobial activity. [51]

2. **Reactive Oxygen Species**

In general, they consist of volatile oxygen free radicals such as superoxide ($O_2^{\bullet -}$) anions, peroxide ($O_2^{\bullet -2}$), hydroxyl ions (OH^-), and hydrogen peroxide (H_2O_2), as well as non-radicals such hydroxyl radicals (•OH) [52]. Oxidative stress may be brought on if the production of ROS exceeds the antioxidant capability of microbial cells. Proteins, fats, RNA, and DNA are examples of intracellular macromolecules that might be harmed by this kind of oxidative stress. The antibacterial power of various ROS varies. The ROS OH−, H_2O_2, and O_2•− are frequently studied in relation to antibacterial action. Some negative ROS, for example OH−, are likely to react with positive charged bacterial cell barriers, but H_2O_2 is further effective in all-pervading cell membranes [53]. It's interesting to note that according to one paper, ROS may both simultaneously break intracellular biomolecules and preserve cell membrane integrity [54]. Ion released by NPs in humid environments can cause the production of ROS. In both extracellular and intracellular contexts, Ag NP-released electrons have been seen to cause bursts of ROS [55]. Biomolecules can be destroyed by the oxidative stress caused by excess ROS; yet, when a ROS scavenger such acetyl cysteine is introduced, the antibacterial effect of Ag NPs is significantly reduced, indicating that bacteria are susceptible to killing by NP-induced excess ROS generation.

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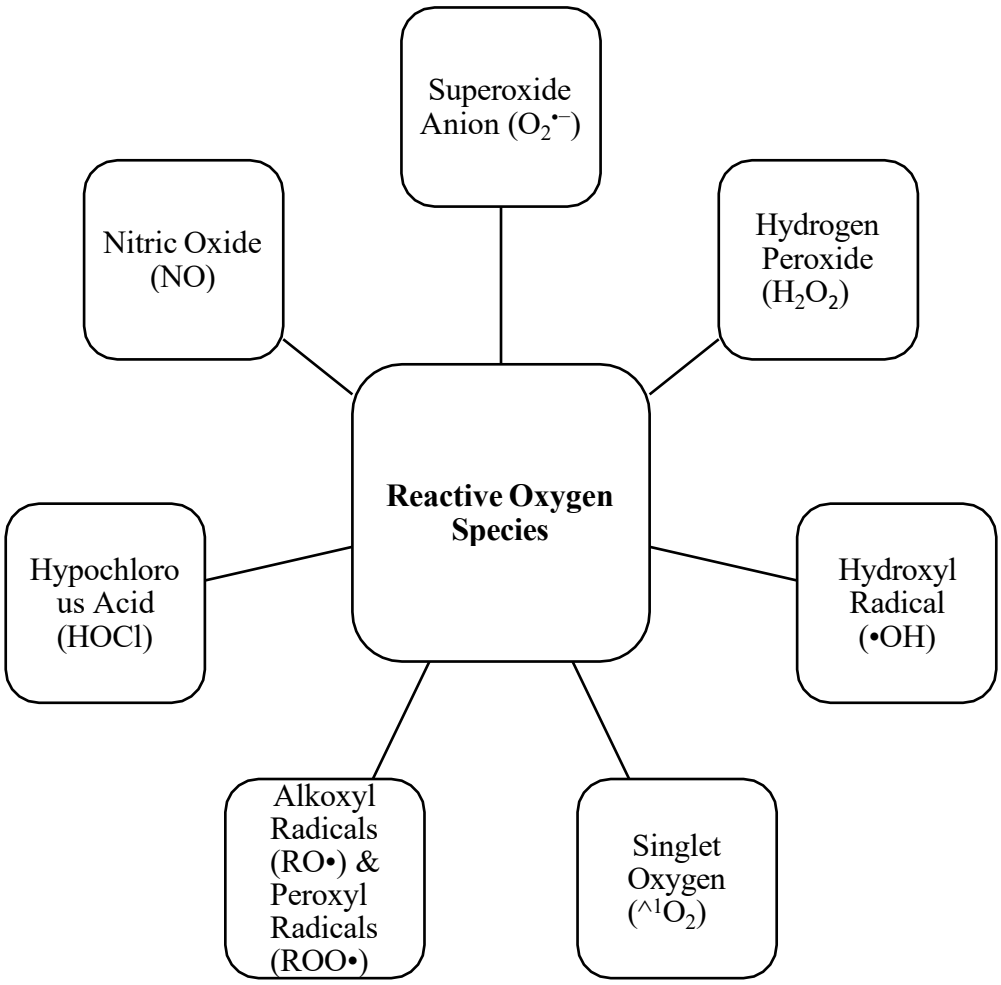

Figure 5: Types of Reactive Oxygen Species (ROS)

3. Killing

Direct contact appears to be a possible antibacterial route, since some study has shown that NPs have antimicrobial characteristics when exposed to dry environments [56,57]. Since NPs' surfaces do not undergo any electrochemical reactions in a dry environment, no ions or electrons are produced to interact with biomolecules or cause ROS explosions. Cu NPs are thought to infiltrate bacterial cells, interact with membrane proteins, and cause an explosion of reactive oxygen species (ROS) in the intracellular environment. Studies have demonstrated that ions cannot be produced to boost Cu NPs' antibacterial activity [58].In certain investigations, it was discovered that Ag NP had strong antibacterial capabilities in situations when Ag ions were not discernible [59]. The antibacterial efficiency of Ag NPs and ions were also compared in control tests, and the results show that NPs were highly efficient than ions in case of *E. Coli* [60]. According to research, the antiseptic activity of Ag NPs of different sizes varied, but their released ion concentrations were almost the same, suggesting that contact killing was the main antiseptic mechanism [61].

An additional illustration, based on a contrast of colloidal and immobilized Ag NPs [62], also implied that contact killing was the predominant antimicrobial mechanism.

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4. **The Consolidated Antimicrobial Process**

Antimicrobial action of NP does not seem to be contingent on any one specific theory. Instead, it is important to take into account the previously mentioned processes (NPs, released ions, and ROS), some of which may work in concert with one another to enhance the antimicrobial process. Regarding to this theory, all may concurrently make use of their own distinct functions. For instance, Ag NPs may build up on the membranes and cell walls of bacteria and control membrane proteins [63], altering the permeability of the membrane to allow the entry of ions and Ag NPs into the cells of the bacteria. Once within cells, Ag NPs continue to produce ions that can damage DNA and proteins. Ag ions cause intracellular ROS, which can potentially damage DNA and proteins.

5. **Immuno-Stimulatory Effects**

NPs have the ability to augment innate antimicrobial immune defenses and alter immunological responses in addition to directly killing [64]. Similar to ROS, reactive nitrogen species (RNS) play an important role in the antimicrobial process. Cu NPs and Ag NPs can raise the concentration of nitric oxide, one type of RNS, which strengthens the host immune system's resistance against microorganisms [65]. Additionally, Cu found in bacteria's protective proteins can be oxidized by nitric oxide to release Cu ions, increasing the toxicity of the compound to microbial cells. Antimicrobial peptides, which are numerous naturally occurring antibiotics generated by humans in addition to RNS, are important antibiotics in the immune system [66]. One kind of antimicrobial peptide, polymyxin B, has synergistic antibacterial activity with Cu and Ag NPs [67]. In order to enhance the immune response, adjuvants are frequently utilized in vaccine manufacture [68].Ag NPs have the ability to significantly raise antigen-specific IgE and IgG1/IgG2a ratios when employed as vaccination adjuvants. Native leukocytes, predominantly macrophages, are also stimulated by Ag NPs [69]. Despite the fact that NPs' immune-stimulatory impact has been suggested as a potential antibacterial process, there are currently few pertinent findings.

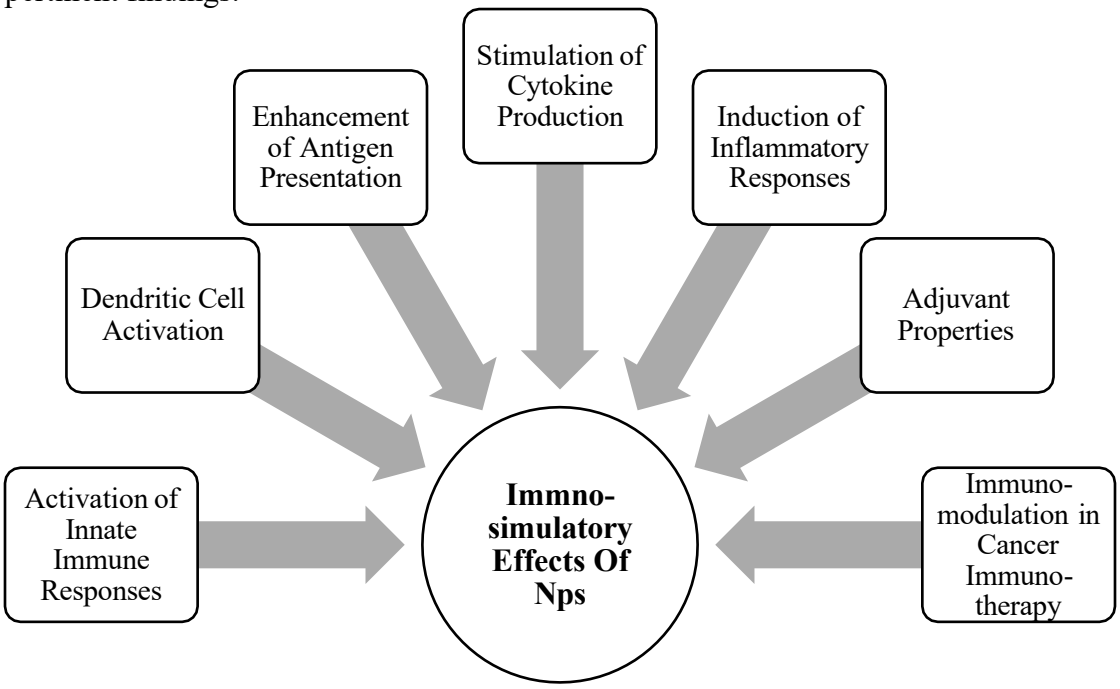

Figure 6: Possible Immunostimulatory Effects of Nanoparticles

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Nanoparticle Type	***Synthesis Method***	***Role in Fighting Antimicrobial Resistance***	***References***
Silver nanoparticles	Chemical reduction, green synthesis	Antibacterial and antifungal activity	73
Gold nanoparticles	Citrate reduction, seed-mediated growth	Drug delivery, antimicrobial agents	74
Zinc oxide nanoparticles	Sol-gel method, hydrothermal synthesis	Antimicrobial and wound healing properties	75
Titanium dioxide nanoparticles	Sol-gel synthesis, hydrothermal method	Photocatalytic antibacterial activity	76
Copper nanoparticles	Chemical reduction, electrochemical deposition	Antimicrobial and anti-biofilm activity	77
Iron oxide nanoparticles	Co-precipitation, thermal decomposition	Magnetic hyperthermia for bacterial eradication	78

Table: Types of Nano Particles, Their Synthesis and Role to Fight Antimicrobial Resistance

Utilizing nano-particles as anti-viral agent

During the development in modern medicine, scientists have begun using nanoparticles for various treatments of various diseases that are rather difficult to cure. Viruses are those particular microbes but with the introduction of several oxides (gold, silver, platinum) to the viral pathogen it appears that the microbe's mechanism has been inhibited and thus prevented the progression of pathogenesis [70]. These are mostly transition metals that are ligands in nature and when come in close proximity of the viral coating the Nano particles disrupt the molecular configuration of the virus along with the inhibition of enzymes and genetic molecule (DNA/RNA) during the insertion cycle. There is also the process of oxidation stress [71] and non-oxidation mechanisms. [72] That produces significant evidence for the viral progress.

The effectiveness of nano particles is dependent on the ability it has to eliminate any type of viral threat which is primarily designed for. The structure and the chemical properties the compound can provide will determine the effectiveness of the medication in use. The first

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category to determine the usefulness in the uptake of the nano particles in cellular tissues [84]. The uptake of the nanoparticles is about 50nm and any smaller will contribute to the uptake into the cell. This is particularly useful in combating HIV infected cells which is derived from the protein TAT [85]. Other factors that determine the uptake is the shape of the nano particles that squeeze through the cell. Antigenicity is also important in the determination of the effectiveness of the nano particles. These compounds (Example PEG) are very important for the effectiveness of the medication as these compounds promote clearing activity against foreign nano particulates (not nano particles) to be inoculated in *vivo*. These compounds prioritize to expel or at the very least deny any viral microbes or any microbes to penetrate the cells [86]. These are just some of the properties by the selective nano particles and many more are being developed to outline more properties with further research. As more research are being conducted on various metallic nano particles including capsuled delivery system various medical products are available to the masses for treatment and therapeutic use. An example is the inhibition of the virus HIV-1 from progressing in the cell via the use of silver particles to inhibit various functions of the viral agent as well as shows many inhibitory actions in *H1N1 influenza* virus [87]. In the resent year of 2020 at February the 8th the new and mutated form of the *SARS virus* was introduced to the world as the new variant known as *SARS cov-2* or the novel Corona virus. This virus was especially difficult to treat with regular vaccine protocol as it was very limited in its function due to the rapid mutation of the genetic information. Scientists then re-evaluated the virus and thus introduced nano particles to prevent the viral infection. With numerous successive case studies regarding the use of metallic nano particles especially silver (AgNP) against influenza, Hepatitis and even small pox researchers introduced this regent to virus for testing [88] it was observed that the AgNP inhibit the progression of the virus by blocking the antigen sites on the cells to prevent attachment to the cell and thus prevent infection. This breakthrough introduced further research to analyze the process. The research found that the reagent also reduces the expression of the Col 1a1 and Col 1a2 genes that confirmed that nano particles will also inhibit gene expression in the cell thus stop pathogenesis and thus eliminate cytokine-based inflammation [89].

Nanotechnology in medicine

Nanotechnology is on the forefront of medical advancements, significantly enhancing the variety and accessibility of drug or drug-like molecules for patients. Nanoparticles act as sheltered carriers for hydrophobic drugs and therapeutic substances like mRNA, siRNA, and DNA, which typically face bioavailability challenges. [90] Nanotechnology ,which is the molecular level manipulation of materials, is a quickly progressing interdisciplinary field with noteworthy potential in communications ,medicine, genomics, and nanorobotics. Past the profitable miniaturization of components, nanoscale objects exhibit extraordinary self-ordering and assembly behaviors governed by distinct forces. Exploring and understanding these unique behaviors will likely lead to innovative approaches that enhance human life. [91]

Current methods for diagnosing and treating diseases

Approaches for detecting and curing ailments, particularly cancer, face significant limitations like low sensitivity, specificity, and drug toxicities. There is ongoing development of advanced cancer detection techniques using nanoparticles, serving as luminescent materials, contrast compounds, chemical instruments, and medications with targeted antibodies. Quantum dots, paramagnetic NPs, nanosomes & nano-shells are among the NPs utilized for diagnostics. Nanotechnology makes it possible to provide extremely hazardous medications with better safety profiles, such cancer chemotherapeutics. These drugs can be targeted specifically to the

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affected tissue through both active and passive means. Additionally, alternative therapeutic approaches, like heat-induced cancer cell ablation using Nano shells and gene therapy, are also under exploration. [92]

1. **Engineered Nanomaterials**
   Engineered nanomaterials are described as having no less than one dimension below 100 nm. In the context of medicine, this definition is adaptable and may encompass a Nano drug featuring particles exceeding 200 nm. Additionally, the term 'nanoparticle' is broad and covers both organic (like lipids and biopolymers) and inorganic Nano substances (such as metals, oxides, and carbon) that can take various shapes like cubes, stars, needles, spheroids, or intricately designed geometries in DNA or protein nanotechnology, as long as they are smaller than 100 nm in aerodynamic diameter. [93]
2. **Nanocarriers Used in Drug Delivery System**
   NNI defines nanoparticles as structures with dimensions between 1 and 100 nm in at least one direction. Despite the term "nano" often being applied to particles equal to quite a few hundred nanometers, nanocarriers with improved properties are more easily absorbed by cells than bigger molecules. Consequently, they prove effective as delivery vehicles for existing bioactive compounds. [94]
3. **Liposomes**
   Liposomes, originally investigated for their role as carriers for drugs, are colloidal carriers typically sized between 80 to 300 nm. These microscopic spherical vesicles are formed spontaneously when certain lipids disperse in water-based solutions, often through processes like sonication. Liposomes are made up of phospholipids, cholesterol, and bilayers or surfactants, and they are recognized for their ability to improve drug solubility. [95]
4. **Nanoparticles Based on Dense Phospholipids**

   Solid lipid nanoparticles (SLN), nanostructured lipid carriers (NLC), and lipid drug conjugates (LDC) are carrier platforms that utilize solid lipid matrices, which remain solid at physiological temperatures. These systems have been utilized for delivering substances via various routes including dermal, oral, injectable, ocular, pulmonary, and rectal routes. SLN comprises solid lipid particles such as purified triglycerides, complex glyceride mixtures, or waxes, stabilized by a variety of surfactants. [96]
5. **Polymeric Nanoparticles**
   Polymeric nanoparticles (pNPs) are made of natural polymers including albumin, DNA, chitosan, and gelatin, or synthetic polymers like poly-ε-caprolactone, polyacrylamide, and polyacrylate. They have diameters between 10 and 100 nm. PNPs can be classified as either non-biodegradable compounds like polyurethane or biodegradable ones like poly(L-lactide) (PLA) and polyglycolides (PGA) based on their in vivo behavior.[97]
6. **Dendrimer Nanocarriers**
   Advanced nanostructures called dendrimer nanocarriers are used for a variety of purposes, including the delivery of drugs. Dendrimers are polymers that are extremely branched and have symmetrical, well-defined structures that resemble trees. Dendrimers' special characteristics allow them to encapsulate medications or therapeutic substances on their surface or inside their internal spaces. This encapsulation improves the payload's stability and solubility while shielding it from deterioration. Additionally, dendrimers can be designed to release the payload in a precise way, providing targeted or prolonged drug delivery. In a

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number of biological fields, such as cancer treatment, gene transfer, imaging, and diagnostics, dendrimer nanocarriers have demonstrated potential.[98]

7. **Silicon Materials**

Silicon materials employed in precise medicine distribution systems fall into categories such as MSNs (Mesoporous Silica Nanoparticles) & xerogels, for instance, Mobil Composition of Matter MCM-41 (MCM-41) and Santa Barbara University mesoporous silica material (SBA-15). These materials offer various benefits as carriers, such as compatibility, a highly permeable construction, and ease of functioning. [99]

8. **Carbon Nano-materials**

Carbon nanocarriers engaged in medicine distribution systems are categorized into nanohorns (CNH) & nanotubes (CNTs). CNTs have a characteristic structure created by the rolling of single SWNCTS (single-walled carbon nanotubes) or multiple mwCNTs (multi-walled carbon nanotubes) coats of graphite, offering a vast surface area and impressive conductivity. Enhancing the nanotubes compatibility can be achieved through chemical modifications to their exterior. [100]

9. **Magnetic Nanoparticles**

Magnetic nanoparticles demonstrate diverse characteristics, rendering them exceptionally favorable as carriers for drug delivery. Notably, these include convenient manipulation through an external magnetic field, the potential for retaining both active and passive drug distribution approaches, the capability of imagining (utilized in MRI), and improved absorption by the objective tissue, leading to active treatment at therapeutically ideal amounts. [101]

Use of nanobiotics to help overcome the antimicrobial challenge

Antibiotic pharmacokinetics can be improved, most notably by encasing the medication in nanoparticles (NPs), which can help reduce toxicity. Developing drug delivery systems, focusing on antimicrobial-resistant enzymes, addressing bacteria resistant to antibiotics, employing physiochemical techniques, and investigating non-traditional approaches to combat multiple drug-resistant organisms are just a few of the alternative strategies that use nanotechnology to produce unique nanomaterials having broad antibacterial activity [103]. The fact that NPs can transport traditional medicines in addition to having bactericidal qualities makes them promising.

Nanotechnology to rescue AMR issues

A durable solution to the aforementioned problems can be found in emerging nanoscale materials and technology because of the distinct way that nanomaterials work against harmful germs. When compared to the usage of antibiotics in bulk, "antibiotic nanocarriers" created on terpenoid ,liposomal, solid/lipid, dendrimeric, polymeric and inorganic elements have demonstrated good results in refining the over-all performance of antibiotics [104].

This was achieved by improving the drug's pharmacokinetics, leading to an extended serum half-life of the antibiotic and a reduced apparent volume of distribution, which is believed to target the infection site more effectively and eradicate pathogens even at minor medicine doses. The combined or synergistic effect of two or more nanoparticles forming hybrid structures, or incorporating multiple drugs within a single nanostructure, enhances pharmacological responses and boosts antibacterial efficacy while mitigating the development of resistance. Nanomaterials exhibit novel and unique mechanisms of action against antimicrobial-resistant strains that differ from the typical bacterial defense mechanisms. [105].

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Toxicity and dose optimization of antimicrobial nanoparticles

RBC lysis and disruption of blood coagulation pathways can be caused by nanoparticles and their hazardous byproducts. High toxicity of AgNP has been shown in in vitro research, and their accumulation can cause dysfunction of important organs such as the lungs, spleen, liver, colon, lymphatic system , and bone marrow in vivo (as well as through intravenous and inhalation usage of NPs in patients) [106]. Silver has been detected in blood and urine and can seep out of wound dressings. Al_2O_3 NPs produce neurotoxicity through interactions with several intra- and intercellular biomolecules.

Future aspect

The future of nanobiotechnology against antimicrobial resistance (AMR) at an industrial scale holds promising prospects, with ongoing and anticipated advancements in modern research. Several key areas suggest potential developments in the role of nanobiotechnology in addressing AMR. Advancements in Nanomedicine may lead to tailored treatments in accordance with distinct microbial profiles. Precision targeting of specific pathogens could improve therapeutic results and lessen the hazard of resistance. Integration of smart nanomaterials with responsive and adaptive properties could enhance targeted drug delivery. Stimuli-responsive nanocarriers might release antimicrobial agents in response to explicit signals, improving treatment precision. Future research may explore synergistic effects by combining multiple antimicrobial agents within nanocomposite structures. Combinatorial approaches could minimize the likelihood of resistance emergence through diverse mechanisms of action. Nanoscale imaging technologies may enable more detailed and accurate diagnostics for rapid detection of resistant strains. Real-time monitoring at the molecular level could revolutionize the understanding of AMR dynamics. Research in nanorobotics might lead to the development of tiny robots skilled at targeted intervention at the cellular or microbial level. These Nano-robots could deliver precise treatments and potentially eliminate resistant pathogens. Integration of bacteriophages (viruses that infect bacteria) with nanotechnology may offer a natural and highly specific approach to combating bacterial infections. Phage-based nanotherapeutics could provide an alternate to outmoded antibiotics, reducing the risk of resistance. Nanobiotechnology may play a crucial role in mitigating AMR in the environment. Nanomaterials could be employed for the efficient removal of antimicrobial residues from water sources and agricultural runoff. Integration of machine learning and artificial intelligence algorithms with nanobiotechnology could help predict resistance patterns. Data analytics may guide the design of more effective nanotherapeutics based on evolving resistance profiles. Future efforts may focus on international collaborations to address AMR challenges collectively. Shared research resources and expertise can accelerate the development and implementation of nanobiotechnological solutions on a global scale. The establishment of regulatory frameworks and standardization for nanobiotechnological interventions against AMR will be crucial for their widespread adoption. Ensuring safety, efficacy, and ethical considerations will be dominant in the progress and deployment of nanotherapeutics.

Can microbes develop resistance against nanoparticles?

Research on resistance to nanoparticles, including various types such as metallic nanoparticles and metal oxide nanoparticles, is a complex and evolving field. Here's a general overview with references to some key studies up to that point. Panáček et al investigates the development of bacterial resistance to silver nanoparticles, a commonly studied type of antimicrobial nanoparticles [107] while Stewart & William Costerton provides insights into antibiotic resistance in the context of biofilms, a scenario that can be relevant to the study of resistance to

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antimicrobial nanoparticles [108]. Furthermore, understanding the possible emergence of immunity to nanoparticles may be aided by Pamela et al.'s discussion of the evolutionary elements of antibiotic resistance [109]. It's crucial to remember that the field of study on resistant nanoparticles is one that is always changing, and future research might offer further information. Furthermore, the kind of nanoparticles used, the target microbes, and the experimental setup can all affect the particular pathways and variables impacting resistance.

Ai and machine learning and nanoparticle potential against AMR

The cutting-edge fields of nanotechnology and computational intelligence including machine learning (ML) have great potential to solve the worldwide problem of antibiotic resistance (AMR). Design and optimization of nanoparticle-based AMR solutions are aided by the quick analysis of large datasets made possible by the combination of algorithmic intelligence and machine learning models. AI can help identify the ideal nanoparticle characteristics—such as shape, size and surface properties—to improve their antibacterial activity using predictive modeling. Additionally, by customizing nanoparticle solutions to target certain drug-resistant strains, deep learning algorithms can support the creation of tailored treatment regimens. By speeding up the development and use of novel antimicrobial drugs based on nanoparticles, the combination of AI, machine learning, and nanotechnologies presents a potent strategy to combat antimicrobial resistance (AMR). This interdisciplinary association embraces the prospective to revolutionize our capability to fight infectious diseases and defend public health in an age of snowballing antibiotic resistance.

Conclusion

In end, the part of nano-biotechnology in contradiction of antimicrobial resistance (AMR) signifies an auspicious frontline in the battle against infectious diseases. Innovative strategies are needed to combat the growing danger of antimicrobial resistance (AMR), and at the nexus of nanotechnology and biomedicine, nano-biotechnology presents special answers. Researchers have created new tactics to fight drug-resistant bacteria thanks to the creation of nanomaterials and nanostructures. The use of nanobiotechnology in the battle against AMR has various benefits. First off, nanoparticles can overcome any resistance mechanisms that microbes may have evolved, increasing the efficacy of already available antimicrobial medicines. Furthermore, nanocarriers can enhance medication delivery by guaranteeing the precise and regulated release of antimicrobial drugs. This reduces the negative effects of traditional therapies while simultaneously increasing therapeutic efficacy. Additionally, the creation of cutting-edge monitoring and diagnostic tools for the early identification of resistant strains has been made possible by nanobiotechnology. Rapid and sensitive detection methods are provided by nano-based biosensors and imaging techniques, enabling for timely intervention and precise management of infections Notwithstanding the promising progressions, challenges such as biocompatibility, toxicity, and long-term effects of nanomaterials need to be carefully addressed. Ethical deliberations surrounding the use of nanotechnology in medicine also deserve cautious examination to safeguard liable and safe disposition.

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