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Review Article on Inorganic Nanoparticles as Antibacterial Agents

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Abstract: ***Pathogenic bacteria are those bacteria that produce illness. These bacteria can cause diseases and infections when they get in the body of a healthy host and begin to reproduce very fast in the host body. For these bacterial diseases, researchers have developed antibacterial agents to aid infectious diseases, which are designed as promising chemotherapeutic agents. But the superbugs are smarter to develop resistance phenomenon against almost all the available antibacterial agents & hence make them ineffective. So there is an unmet need to develop antibacterial which do not develop fast resistance & can kill the superbugs so as to save the humanity against the cruel clutches of these superbugs. In this review, we discussed the recently discovered novel antibacterial based on inorganic nanoparticles.***

Abbreviations/Symbols/Formula: NP's=nanoparticles, MgO=Magnesium oxide, ZnO=Zinc oxide, Ag=Silver, Au=Gold, Cu=Copper, Al=Aluminium, Ni=Nickel, TiO_2=Titanium oxide, ZnS=Zinc sulphide, ROS=reactive oxygen species, S.=Staphylococcus, E.=Enterococcus, NADH= Nicotinamide Adenine Dinucleotide dehydrogenases.

Keywords: Antibacterial, inorganic nanoparticle, infectious diseases, superbug.

I. INTRODUCTION

Bacterial infections is one of the most important infectious diseases. From last 50 years of expanded research, scientists described many novel antibacterial medicines isolated from different sources to cure these diseases. But superbug seems more powerful.

Besides all the efforts of the scientists, there is still an urgent unmet need to develop new antibacterial agents to overcome the damage caused by the superbugs who has developed

mutations & mechanisms to overcome the effect of the existing antibacterial & hence has become multidrug resistant bacteria.[1]

Antibacterial agents can be classified as bactericidal which kill bacteria and bacteriostatic which slow down the bacterial growth. It is sometimes a very difficult process to find a clear boundary between these two antibacterial agents like bacteriostatic and bactericidal. Particularly when high concentration of some bacteriostatic agent is used, then they may work as bactericidal.[2]

Resistance can develop across many antibacterial agents.

Furthermore, many drawbacks for common antimicrobial agents are not only the development of multidrug resistance, but also there is an adverse side effects due to this resistance. But drug resistance impose high dose of antibiotics always generating toxicity. This causes the development of different strategies to act towards bacterial diseases.[3] Nanoscale materials like Nanoparticles appear to be as new antibacterial agents.

Further we discuss various types of inorganic nanoparticles which act as antibacterial, their mechanism of action followed by their methods of preparation.

There has been an extraordinary growth in field of nano science and technology. The development of new techniques to synthesise nanomaterials and the accessibility of tools for the classification and manipulation of nano-particles[4] have lead to a steep technological rise giving new nano size antibacterial agents with improved chemical, physical and biological properties.[5]

A. Classification of Inorganic Nanoparticles

Various types of Inorganic Nanoparticles have been made & based on the nature of its constituents. They can be classified as either Metal nanoparticles or Metal oxide/Metal sulphides nanoparticles. The Metal nanoparticles are generally made up of transition metals like Ag , Au, Co, Ni, Cu, Fe although a few exceptions are known, for example, nanoparticles of Al metal is also known which is a *p*-block metal. The Transition Metal oxides include oxides of all the groups of the periodic table including *s*-block metals as well as *p*-block metals like CuO, Cu_2O, ZnO, MgO, Al_2O_3, TiO_2, SiO_2 nanoparticles. Even a Metal sulphide like ZnS is also known to form an antibacterial nanoparticle. Based on their magnetic properties they can also be classified as Magnetic or Nonmagnetic nanoparticles.

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II. METAL NANOPARTICLES

A. Ag Nanoparticle

Perelshtein et al. 2008 observed that the mostly used antibacterial nanoparticle is Silver which is produced in a way that effects a large area and used in various fields; to eliminate microorganisms on textile fabrics and to reduce infections in burn treatment.[6] The effectiveness of silver compounds made them to act as an antiseptic. This is based on the ability of the silver ion (Ag^+) to reach to the cell membranes of pathogens to irreversibly damage their key enzyme systems, making it an ideal biocidal agent.[7] The treatment with silver nanoparticles was observed by Raffi *et al*.(2008) and Sondi & Salopek-Sondi (2004) & are responsible for the changes in the bacterial cells. These changes are considered as the cause of cell death. They observed the presence of condensed silver nanoparticles in the membrane of *E. coli* cells and NP's were found to stick inside bacterial cells.[8] Elham Ghaderi and Omid Akhavan found that an electric field generation was responsible for the antibacterial activity of silver nano-rods against *E. Coli* bacteria.[9]

B. Al Nanoparticle

Aluminium nanoparticle are synthesized by all three, solid phase synthesis (mechanical ball milling, mechanochemical synthesis), liquid phase synthesis (laser ablation, exploding wire, solution reduction and decomposition processes) and gas phase synthesis (gas evaporation). Yamamoto *et el.* synthesised Al NP's using laser ablation method in argon gas as ambient gas. They found that it is possible to control the particle size synthesised by controlling the ambient gas temperature. Alumina nanoparticles exhibit the antibacterial activity which is due to the release of metal ions. Jiang *et el.* observed that dissolved metal ions were not present in a measurable quantity in the airy medium of the suspension. They observed in pH studies that alumina particles were positive while bacterial surface was found to be negative. Because nanoparticles are attached to the surface of bacteria due to the surface charge, thus the aluminium ions in nanoparticles mediated toxicity.[10]

C. Au Nanoparticle

Gold nanoparticles related to the behaviour of biomaterials are easily found to be conjugated with biomaterials for treatment of cancers, gene therapy, detection, imaging, diagnostic and have therapeutic applications in many other diseases.[11] Platinum based drug delivery was used as a frame for gold nanoparticles, because these NP's would be non-toxic and non-immunogenic.[12-15] These type of platinum drug are also attached with the targeting groups, like peptides and aptamers which increase the selectivity towards lung cancer. The most preferable spots for gold nanoparticles attack are those when they attack with phosphorus or sulphur holding bases. Thus respiratory chains are broken when gold nanoparticles are attached to sulphur containing groups of enzymes (NADH) with the generation of large amount of free radicals which may lead to cell death.[16] The biocidal potential of Gold NP's were investigated by Robert Koch..[17]

D. Cu, Ni & Cu-Ni Nanoparticles

Copper nanoparticles exhibit antibacterial activity mainly due to the stickiness with bacteria . This attachment occur due to the presence of opposite electrical charges which results in reduction of reaction potential at the cell wall of bacteria.[18]

This type of nanoparticles also exhibit bactericidal effect against S. Aureus, E. Coli and S. Mutants. For Nickel NP's and bimetallic Cu–Ni NP's they exhibit only a bacteriostatic effect on the same microorganisms.[18]

III. METAL OXIDE NANOPARTICLES

A. MgO Nanoparticle

Magnesium oxide also act as antibacterial agents. There are many methods for preparing magnesium oxide nanoparticles. It can be prepared by green synthesis methods by extracton of neem leaf using Magnesium nitrate. It can also be prepared by sol-gel method, microemulsion method, hydrothermal methods etc.[19]

Hewitt *et al.* (2001) investigated that magnesium oxide nanopowder exhibit antibacterial activity against E. coli. This antibacterial activity was due to the formation of superoxide ion which was formed by the surface of magnesium oxide powder.[20] Another researcher Krishnamoorthy *et al.* (2012) also reported that the antibacterial activity of magnesium oxide against the gram negative bacteria.[20] Stoimenov *et al.* (2002) investigated the cause of cell death which was due to electrostatic interaction between magnesium oxide nanoparticles and the bacterial surface. Peter *et al.* (2002) and Makhluf *et al.* (2005) also observed the same that nano-magnesium oxide shows high activity against bacteria. This activity was due to the interaction of particles and bacteria. Sawai *et al.* investigated the antibacterial activity of magnesium oxide nanoparticle which formed a thin layer around the particles. This formation of layer was due to the saturation of water moisture on the surface.[20]

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B. ZnO Nanoparticle

Nanomaterials exhibit antibacterial activities by interacting physically and chemically. Shinde *et al.* observed the formation and particle size of zinc oxide nanoparticles which can be controlled by changing the power of microwave and time of the reaction. Some Scientists synthesized nanotubes which have wall thickness less than 2 nm with a hexagonal inner as well as outer wall.[21]

For the growth of one dimentional Zinc oxide nanostructures Ramani *et al.* observed the effect of concentration of pyridine as base as well as a capping agents.[22] ZnO nanorods synthsized by hydrothermal method through a seeded solution was evaluated by Jansson *et al.*[23]

Surfactant free synthesis was done by Talebian *et al.* They obtained flower like formation for various solvents like hexanol, ethylene glycol and water.

This synthesis of zinc oxide nanostructures were also obtained with use of nano rods and spheres.[24]

Preparation of zinc oxide particles with polyvinyl chloride resulted in growth reduction of *S. Aureus* which was observed by Seil *et al*.[25]

C. CuO, Cu_2O Nanoparticles

The antibacterial activities of copper(II)oxide and copper(I)oxide were discussed in various reports related to the formation of copper ions, dissolution of copper ions and their size effect in various medium. Due to the degradation of molecules these Cu (I) and Cu (II) ions generate superoxide species in bacterial cells. In this Cu(II) ions are reduced to cuprous Cu(I) ions, this reduction of ions is due to the driven ROS which is responsible for causing oxidative stress.[26]

In the literature antibacterial potency of Cu_2O over CuO has been noted, which is due to release of ionic Cu from metallic Cu surfaces.[27]

D. TiO_2 nanoparticles

The antibacterial activity of titanium oxide nanoparticles were observed against E. coli (Gram negative). Titanium oxide nanorods are very useful in biomedical applications. Synthesis of TiO_2 nanorods were done by using hydrothermal process. Analysis of titanium oxide nanorods were done by Scanning Electron Microsocope, Transmission Electron Microscope, X-Ray Diffraction. All the instruments gave the same result that TiO_2 nanorods are crystalline in nature.[28]

E. Al_2O_3 nanoparticles

The aluminium oxide nanoparticles showed their antibacterial properties on both gram negative and gram positive bacterial strains. Due to the formation of the zone of inhibition, the scientists concluded that aluminium oxide is a good antibacterial agent.[29]

F. Silica Modified Nanoparticles

Nitric Oxide silica particles have been used to control the antibacterial activity against E. coli and Pseudomonas aeruginosa. Various methods have been developed to control the biofilm formation and to deliver Nitric oxide to bacteria, but authors found that the *N*-Methylaminopropyltrimetoxysilane silica nanoparticles had 1000- fold greater efficacy against P. Aeruginos biofims than *N*-(6-inohexyl)aminopropyltrimethoxysilane nanoparticles.[30]

IV. METAL SULFIDE NANOPARTICLES

A. ZnS Nanoparticles

The antibacterial activity of zinc sulphide was observed by Kanemeto *et al.* They also observed the photocatalytic and photophysical properties of ZnS nanoparticles. Observation was done with the help of photoluminescence (PL) study. The peak was obtained at 325 nm (3.85 eV), which occur due to the transition of electrons to valence electrons. They measured PL emission at various wavelengths.

They also checked PL spectra for all samples and observed broad peak at 363 nm and 220 nm peak at excitation of wavelength. Broad red shifts took place in the presence of luminiscence and in the absence of band edge luminiscence occur due to unsaturated sp^3 hybridised orbitals of sulphur atoms. Thus it was concluded that capping agents are very useful to remove zinc dangling orbitals from the gap.[31]

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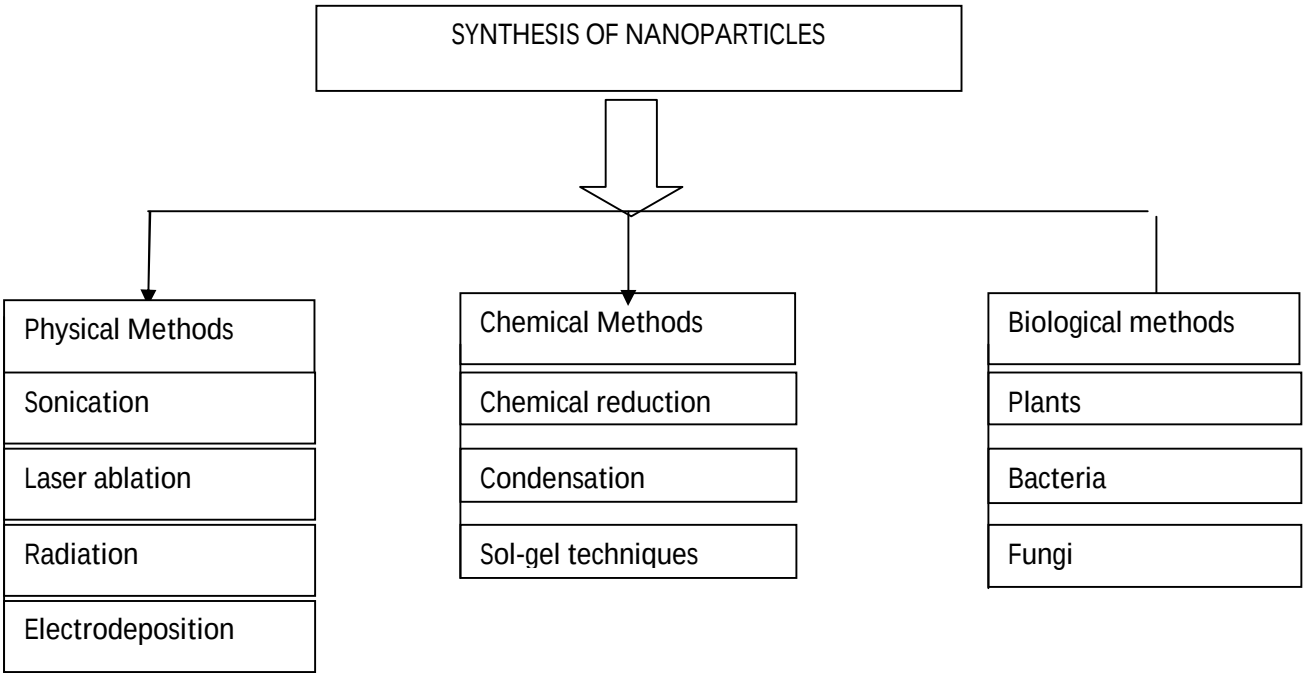
B. Various Methods for Making Nanoparticles

The Inorganic nanoparticles can be conveniently produced by any of the physical or chemical or biological method.



V. CONCLUSION

Various nanomaterials like nanoparticles exhibit various type of antibacterial activity. Many pathogenic superbug bacteria developed resistance and have multiple pathways making them more powerful. To overcome this resistance, formation of various nanoparticles based antibacterial medicines were initiated. This antibacterial resistance is due to long production cycle. Use of poor quality and fake medicines are done in both developing as well as developed country. Nanoparticles have strong potential to kill the bacteria, therefore bacteria cannot develop resistance against them. Most of the nanoparticles are not toxic towards human but are more toxic towards bacteria. Thus nanoparticles act as a novel solution to overcome the resistance and have effective nanostructure to target microbes. Thus there is a great advantage for using them on large scale in future use.

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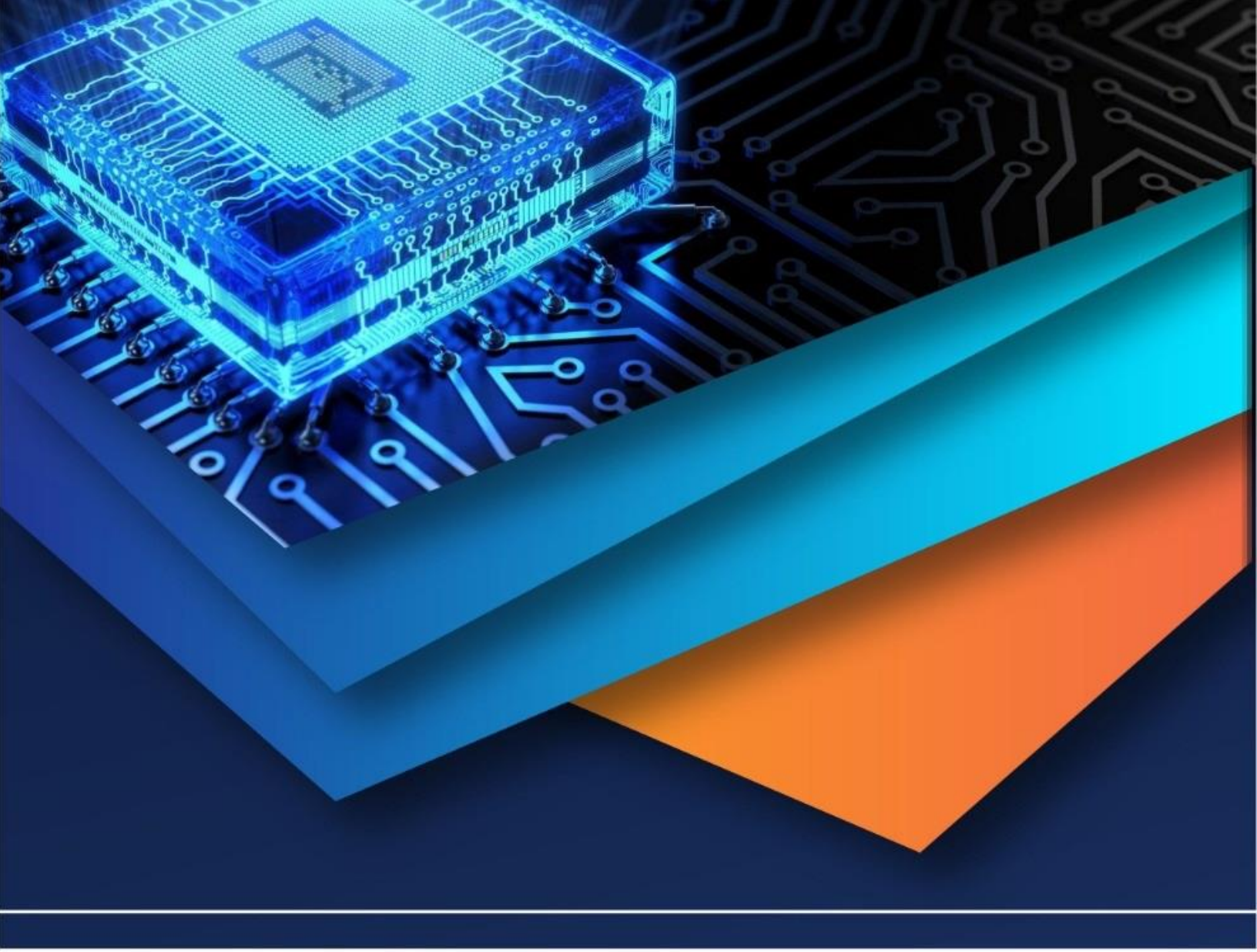

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