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GREEN SYNTHESIS AND ANTIMICROBIAL PROPERTY OF GOLD NANOPARTICLES : A REVIEW

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ABSTRACT

Bacterial infections are still a major cause of morbidity and mortality despite numerous existing potent antimicrobial means. As antibiotics have been used up to a great extent against pathogenic bacteria, many bacterial strains have now developed resistance to those through genetic mutations. To overcome this, Nanotechnology has emerged as one of the most promising and attractive approach in health care industry due to its capability of modulating metals into their nano-size, which drastically changes the chemical, physical and optical properties of metal. Among all metals, gold is a well known biocompatible metal. Gold nanoparticles are of interest mainly due to their stability under atmospheric conditions, resistance to oxidation, and non cyto-toxicity. In recent times, due to the need of safe, clean, nontoxic, and eco-friendly synthesis of nanoparticles, biological or green synthesis is thought to be an advantage over physical and chemical methods. In this review, we have emphasized the green synthesis of gold nanoparticles using fungus, antimicrobial potential of gold nanoparticles, and various mode of action of gold nanoparticles.

KEYWORDS: Gold Nanoparticles, green synthesis, Antimicrobial agents.

INTRODUCTION

Bacterial infections are considered to be major cause of chronic infections and mortality in many cases. Preferred treatment method for bacterial infections is use of various types of antibiotics which are cost-effective and powerful against them. However, several studies have suggested that the widespread and uncontrolled use of antibiotics has led to the emergence of multidrug-resistant bacterial strains. In fact, super-bacteria, which has recently emerged due to abuse of antibiotics, is resistant to nearly all antibiotics. It carries a super-resistance gene called NDM-1.[1] The major groups of antibiotics that are currently in use act by inhibiting the cell wall synthesis, or targeting the translational machinery, and DNA replication machinery. Unfortunately, bacteria can develop resistance against each of these. The mechanisms of resistance include expression of enzymes that modify or degrade antibiotics,[2] modification of cell components, such as the cell wall in vancomycin resistance and ribosomes in tetracycline resistance,[3] and expression of efflux pumps, which provide simultaneous resistance against numerous antibiotics.[4] Unlike, antibiotics, Nanoparticles (NPs) act by targeting the cell wall without penetrating it. This property of NPs raises the hope that it would be less prone to promote resistance in bacteria than antibiotics. Therefore, attention has been focused on this novel and promising NP-based treatment.

Nanoparticles are small clusters of atoms that have at least one dimension in the nanometer scale range (1–100 nm). The broad field of Nanotechnology has emerged as one of the most promising approach to many areas. It's potential to develop nano-sized materials, which are completely different in their physical, chemical and optical properties as compared to their bulk materials, has sparkled immense interest for its application in diverse areas ranging from medicine to engineering.[5] Various metallic NPs have shown broad-spectrum antibacterial properties against both Gram-positive and Gram-negative bacteria. For example, Ag NPs exhibit concentration dependent antimicrobial activity against *E. coli*, and *P. aeruginosa*.[6] The mode of action of NPs is generally described by oxidative stress induction,[7] metal ion release,[8] or non-oxidative mechanisms.[9] These three types of mechanisms can occur simultaneously Moreover, the generation of reactive oxygen species (ROS) inhibits the antioxidant defence system and causes mechanical damage to the cell membrane. Once the membrane is disrupted, it interferes with DNA and proteins synthesis. Certain studies have proposed that some metallic NPs change bacterial membrane penetrability by neutralization of the surface electric charge, leading to cell death.[10]

This review focuses on the green synthesis of Gold nanoparticle (AuNPs) by fungus and their antibacterial activity which has been explored in recent years. Investigation of the antibacterial mechanisms of NPs is very important for the development of more effective antimicrobial materials.

Green Synthesis of Gold Nanoparticles

During the last few years synthesis of gold nanoparticles has gained great significance due to their biological properties. Chemical and physical approaches can also be used in metallic nanoparticles synthesis. However, these methods are expensive and toxic. It is very likely that trace amounts of unreacted reagents used in chemical methods may remain in the solution causing environment pollution. Moreover, nanoparticles synthesized by this may have adverse effects in biomedical applications.[11] Therefore, one of the most crucial needs in nanotechnology is to develop eco-friendly technologies in AuNPs synthesis. The biosynthesis of gold nanoparticles by microbes is thought to be safe, clean, nontoxic, and environmentally acceptable "green chemistry" procedures. AuNPs with well-known size, shape, and morphology can be synthesized by using various microorganisms. AuNPs synthesis can be classified into intracellular and extracellular synthesis depending on the location where AuNPs are formed.

Among microbes, fungus is considered as potent nanofactories. Its high metal tolerance, efficient secretion of soluble proteins and other reducing components, easy scale up, economic viability and easy handling make it excellent candidate for the synthesis of extracellular gold nanoparticles. large amounts of proteins and enzymes secreted by fungi results in larger amounts of nanoparticles being manufactured.[12] Extracellular synthesis of gold nanoparticles is reported using fungi such as *F. Oxysporum,*[13] *Colletotrichum sp*.,[14] *Trichothecium sp,*[15] *Trichoderma koning*[16] and *Penicillium sp*.[17]

Applications of Gold Nanoparticles

Despite its centuries-old history, biological application of gold nanoparticles could only be established in 1971, when the British researchers Faulk and Taylor studied a technique of electron microscopy visualization of the surface antigens of *salmonella* by conjugating antibody with colloidal gold.[18] It is evident by many studies that AuNP conjugates can be used in the treatment of cancer,[19] arthritis[20] and antimicrobial therapies.[21] In a study, it is shown that when cancer cells are treated with biologically synthesized AuNPs under electromagnetic radiations, malignant cells are degraded.[22,23] Their light scattering ability can be used as an alternative contrast mediator in microscopy. Under dark field light scattering, AuNPs can be used to detect metabolites, tumors, endocytosis and receptors in cells.[24] Unique properties of AuNPs such as surface plasmon resonance, surface enhance Raman scattering , magnetic properties (MRI), and fluorescence behavior shown upon conjugation with biological and biocompatible ligands can be exploited for diagnosis and treatment of cancer and human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS).[25] A biosensor based on gold nanoparticles for quantitative measurement of glucose was reported in 2004.[26] Au NPs also have the potential to degrade and detoxify toxic pollutants.[27,28]

Antimicrobial Activity of Gold Nanoparticles

Apart from their other applications, the antimicrobial activity of AuNPs has been mostly exploited.[29] The therapeutic use of gold can be traced back to 2500 BC in China. In the Indian Ayurveda, colloidal gold is still being used for rejuvenation and revitalization during old age under the name of Swarna Bhasma.[30,31] Gold has also been used in the western countries as nervine, a substance that could revitalize people suffering from nervous conditions. In 1920s, bacteriostatic effect of gold cyanide against the *tubercle bacillus* was studied by Robert Koch.[32] The gold is also used in treatment of rheumatic diseases including psoriasis, juvenile arthritis, planindromic rheutamitism and discoid lupus erythematosus.[33] Spherical AuNPs with a variety of surface modification have been proved non-toxic to human cells, despite being taken into them.[34] the efficacy of the antibacterial activity of gold nanoparticles can also be increased by adding antibiotics.[35] A research showed that the coating of aminoglycosidic antibiotics with gold nanoparticles has an antibacterial effect on a range of Gram-positive and Gram-negative bacteria.[36] Infact, it is suggested that Cefaclor (a second-generation β- lactam antibiotic) reduced gold nanoparticles have potent antimicrobial activity on *S. aureus* and *E. coli* compared to cefaclor and gold nanoparticles alone.[38] It also showed that Cefaclor inhibited the synthesis of the peptidoglycan layer, making cell walls porous. Further, the gold nanoparticles generated holes in the cell wall, resulting in the leakage of cell contents and cell death. Considering the advantageous properties, gold nanoparticles are being used to deliver protein based drugs like ampicillin for antimicrobial activities.[38] gold nanoparticles with different anionic groups have been reported to inhibit influenza.[39] Nanoparticles mostly hinder the ionic charges across plasma membranes, resulting in change in permeability of membranes.[40,41] Moreover, nanoparticles also enhance the expression of genes helping in redox processes and thus leading to fungal and bacterial death.[42] This antimicrobial potential is of AuNPS is attributed to its distinctive surface chemistry, smaller size, polyvalent and photothermic nature.[43-45] They generate high amount of free radicals, which interrupt the respiratory chains leading to cell death.[46] Antimicrobial potential of the NPs are affected by the size and surface chemistry.[47] Increase in size will decrease their activity and vice versa.[48] Apart from the size, the antimicrobial activity was also different in case of cell wall composition. In some studies, AuNPs showed highest activity against gram-negative bacteria than gram-positive bacteria, reason being the presence of peptidoglycan in cell wall of the gram positive bacteria thus forming a more rigid structure leading to difficult penetration of the AuNPs compared to the gram-negative bacteria where the cell wall possesses thinner layer of peptidoglycan.[49,50] Other than the size of NPs and cell wall structure of bacteria, surface modification (coating or capping agents) concentration and purification methods also affect the antibacterial activity.[51] It is very interesting that all these green synthesized AuNPs show efficient antibacterial activity against certain bacterial strains, especially compared to chemically synthesized AuNPs which showed nearly no antimicrobial activity against similar strains.[52] The antibacterial activity may be due to the synergistic effect of the combination of AuNPs and extracts.[51]

CONCLUSION AND FUTURE PROSPECTS

Gold nanoparticles have multiple applications in various fields of science such as electronics, disease diagnostics and treatment, imagining, probes, catalytic, remediation and cellular transportation. Despite being synthesized through different physical and chemical methods, biological reduction of the gold salt to synthesize AuNPs has emerged as a winner because of being inexpensive, eco-friendly and safe process. No toxic chemicals or contaminants are produced in this process. Moreover, AuNPs of controlled size and morphology are also synthesized in huge amounts by this method. Bioactive molecules present in these biological resources increase their stability and reduction potential. But detailed study is needed to explore the exact mechanism and metabolites involved in the reduction process. Based on the previously available promising data that demonstrated the antibacterial activity of different metal nanoparticles synthesized using fungi, we believe that this can be a potential candidate for more research into treatments for antibiotic-resistant bacteria. Regardless of their potential, questions are still raised with concerns to the biodistribution of the nanoparticles (NPs) and their possible toxicity to the organism as a whole or at the level of cyto- and genotoxicity. Once explored, it will revolutionize the synthesis of AuNPs on both laboratory and commercial scale.

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