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GREEN SYNTHESIS AND BIOCOMPATIBILITY OF NANOPARTICLES

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ABSTRACT
Nanotechnology (NT) is a field that is mushrooming, making an impact in all spheres of human life. Presently available literature revealed that the NP synthesis using medicinal plants, microorganisms and algae and others as source has been unexplored and underexploited. NT is very important in developing sustainable technologies for the future, for humanity and the environment. The development of green processes for the synthesis of NP is evolving into an important branch of nanotechnology. Green mediated synthesis of metal nanoparticles is gaining more importance owing to its simplicity, rapid rate of synthesis of NP of attractive and diverse morphologies and elimination of elaborate maintenance of cell cultures and ecofriendliness. It has many advantages such as, ease with which the process can be measured up, economic viability and etc. This review presents a summary of green synthesis and biocompatibility of and a concise account of the *in vitro* toxicity data on nanoparticles. Presently, the researchers are looking into the development of cost-effective procedures for producing reproducible, stable and biocompatible metal NPs.
Keywords: Nanotechnology, *In vitro* toxicity, Biocompatible.

INTRODUCTION

The word “nano” is used to indicate one billionth of a meter or 10^{-9}. Nanoparticles are clusters of atoms and their size from 1–100 nm. “Nano” is a Greek word meaning extremely small. Nanoparticles (NP) attract greater attention due to their various applications in different fields including “nanomedicine”. NPs can be broadly grouped into two, namely, organic nanoparticles which include carbon NPs where as some of the inorganic nanoparticles include magnetic NPs, noble metal NP (like gold and silver) and semi-conductor nanoparticles (like titanium oxide and zinc oxide). Metallic nanoparticles are most promising and remarkable biomedical agents. Silver, Aluminum, Gold, Zinc, Carbon, Titanium, Palladium, Iron and Copper have been routinely used for the synthesis of NPs. Materials at the nanometer dimension are not new. NPs are common in nature, for example, life depends on many nanoscaled objects, including proteins, enzymes and DNA, and nanosized particles occur naturally in the atmosphere. Natural sources of nanoparticles include fires and volcanic eruptions. The nanotechnology have short to long term uses like environmental pollution cleanup, efficient and safe drug delivery mechanisms with less side effects, developments in information technology, self-cleaning window glass, ‘smart’ fabrics which adjust to suit the temperature. Some of these technologies have already been adopted. Striving for alternative and cheaper pathways for nanoparticles synthesis, scientists contributed to the development of a relatively new and largely unexplored area of research based on the biosynthesis of nanomaterials[1]. Ultra small particles (USPs, size/diameter <10 nm), so-called “ultra small nanoparticles” are reviewed[2]. Applications of NPs in medical field already explored [3-6]. Scientists are looking for longer-term applications including design of additional ‘smart’ materials such as food packaging which changes color when the ‘use by’ date of its contents expires. NT is important in developing sustainable technologies for the future, for humanity and the environment. There is a growing need to develop environmentally friendly processes through green synthesis and other biological approaches. There are significant concerns associated with the use of NPs. Green mode of synthesized nanostructures have been considered to have better biocompatibility than the chemically or physically synthesized nanostructures. Therapeutic agents can also be coated onto the surface of gold NPs. A key issue in evaluating the utility of these materials is assessing their potential toxicity, either due to their inherent chemical composition or as a consequence of their nanoscaled properties. This review presents a summary of green synthesis and biocompatibility of and a concise account of the *in vitro* toxicity data on nanoparticles.

Importance of the Study

Presently available literature revealed that the metal NPs synthesis using plants, microorganisms and algae as source has been unexplored and underexploited. Resistance to antimicrobial agents by pathogenic bacteria has emerged in recent years and is a major health problem. The development of green processes for the synthesis of NP is evolving into an important branch of green nanotechnology. Plants have evolved in the presence of natural nanomaterials. However, the probability of plant exposure to nanomaterials has increased to a greater extent with the ongoing increasing production and use of engineered nano materials in a variety of instruments and goods. Plant mediated synthesis of metal NPs is gaining more importance owing to its simplicity, rapid rate of synthesis of NP of attractive and diverse morphologies and elimination of elaborate maintenance of cell cultures and ecofriendliness. Physicochemical properties of nanomaterials, biological effects. The unusual physicochemical properties of engineered nanomaterials are attributable to their small size (surface area and size distribution), chemical composition (purity, crystallinity, electronic properties etc.), surface structure (surface reactivity, surface groups, inorganic or organic coatings etc.), solubility, shape and aggregation. Shape of the NPs has been shown to have a pronounced effect on the biological activity. Reactive oxygen species (ROS), due to their high chemical reactivity can react with DNA, proteins, carbohydrates and lipids in a destructive manner causing cell death either by apoptosis or necrosis. The most frequently affected macromolecules are those genes or proteins, which have roles in oxidative stress, DNA damage, inflammation or injury to the immune system. The rapid advancement of nanotechnology has raised the possibility of using engineered NPs that interact within biological environments for treatment of diseases. NPs interacting with cells and the extracellular environment can trigger a sequence of biological effects. These effects largely depend on the dynamic physicochemical characteristics of NPs, which determine the biocompatibility and efficacy of the intended outcomes. As with any other man-made materials, both *in vitro* and *in vivo* studies on biological effects of NPs need to be performed In vitro model systems provide a rapid and effective means to assess NPs for a number of toxicological endpoints. They also allow development of mechanism-driven evaluations and provide refined information on how NPs interact with human cells in many ways. Such studies can be used to establish concentration–effect relationships and the effect-specific thresholds in cells. These assays are suited for high-throughput screening of an ever increasing number of new engineered nanomaterials obviating the need for *in vivo* testing of individual materials.

Significance and Synthesis of NPs Particles

The reason for selecting plant for biosynthesis is because they contain reducing agents like Citric acid, Ascorbic acids, flavonoids, reductases and dehydrogenases and extracellular electron shuttlers that may play an important role in biosynthesis of metal nano particles[7]. They life span of metal nanoparticles and speed up the rate of synthesis in comparison to microorganism's. Depending on the origin we can distinguish three types of NPs, natural incidental and engineered. Natural NPs have existed from earth formation and still occur in the environment in volcanic dusts and mineral composites. The general procedure using plants to produce metallic nanoparticles employs the dried biomass of the plants and a metallic salt, as bioreducing agent and precursor, respectively. The green synthesis of NPs involves three main steps, including (a) selection of solvent medium, (b) selection of environmentally benign reducing agent, and (c) selection of nontoxic substances for the NPs synthesis[8]. Studies have shown that the size, morphology, stability and properties (chemical and physical) of the metal nanoparticles are strongly influenced by the condition of experiment, the kinetics of interaction of metal ions with reducing agents, and adsorption processes of stabilizing agent with metal nanoparticles[9-10] Different materials can be used to make these nanoparticles, such as metal oxide ceramics, silicates, magnetic materials, lyposomes, dendrimers, emulsions and etc.[11]

Factors affecting Biosynthesis of Nanoparticles

Synthesis of nano materials with the required quality and desired properties are one of the important issues in present greennanotechnology. Different kinds of NPs can be successfully synthesized by traditionally chemical and physical methods. Temperature plays an important role to control the aspect ratio and relative amounts of gold nanotriangles and spherical nanoparticles. pH of the medium also influences the size of nanoparticles at great concern. Other than pH and temperature other factors like concentration of extract also play role in NP synthesis and reduction process of ions into metallic nano.

Biocompatibility of NPs

They also serve as well defined systems for studying the structure–activity relationships involving nanomaterials. Some of the distinct advantages of *in vitro* systems using various cell lines include; (1) revelation of primary effects of target cells in the absence of secondary effects caused by inflammation; (2) identification of primary mechanisms of toxicity in the absence of the physiological and compensatory factors that confound the interpretation of whole animal studies; (3) efficiency, rapidity and cost-effectiveness; The cytotoxic effects for almost all kinds of metallic, metal oxide, semiconductor NPs, polymeric NPs and carbon based nanomaterials etc have been reported. For establishing 'safe' nanotechnology it would be necessary to prove non-genotoxic nature of the nanomaterials in question. Several genotoxicity assays can be carried out *in vitro. In vitro* cytotoxicity studies of NPs using different cell lines, incubation times and colorimetric assays with different nanomaterials are increasingly being published. The techniques that can be used to assess toxicity of nanomaterials include (1) *in vitro assays* for cell viability/proliferation using MTT, LDH assay [12-13], mechanistic assays [ROS generation, apoptosis, necrosis, DNA damaging potential] using ROS assay[14-15] (2) microscopic evaluation of intracellular localization [include SEM-EDS, TEM, AFM, Fluorescence spectroscopy, MRI, VEDIC microscopy] (3) gene expression analysis, high-throughput systems (4) *in vitro* hemolysis and (5) genotoxicity etc. The NPs are tested for biocompatility for pulmonary [16], Erythrocytes [17], Endothelial cells for cardiovascular disease [18], Ovarian Cancer [19- 20], in animals spleen injury, Lung inflammation [21], Mouse embryonic fibroblasts [22], Human monocytes [23-24], Human spermatozoa [25], murine glioma cells [26], Ocular use [27].

Applications

Nanotechnology is a field that is mushrooming, making an impact in all spheres of human life. During the current scenario nanotechnology motivates progress in all sphere of life, hence biosynthetic route of nanoparticles synthesis will emerge as safer and best alternative to conventional methods. Recently Sesbania Gum is used to prepare metal NPs and it is a new idea, green and low cost approach for synthesis nanoparticles [28]. Natural polymer *Bombyx mori* silk fibroin is used as a biotemplate to produce silver nanoparticles *In situ* under light (both incandescent light and sunlight) at room temperature it shown an effective antibacterial activity against the methicillin-resistant *S. aureus* and subsequently inhibits the biofilm formation caused by the same bacterium [29].Though various biological entities have been exploited for the production of nanoparticles, the use of plants for the facile robust synthesis of nanoparticles is a tremendous. The use of nanoparticles for biomedical applications, such as drug, delivery, biosensors, cancer treatment, has been extensively studied throughout the past decade [30-39]. Very recently, nanoparticles have gained significance in the field of Biomedicine. Plants and plant extracts can be effectively used in the synthesis of NPs and others as a greener route. Shape and size control of nanoparticles is easily understood with the use of plants. The nanoparticles extracted from plants are used in many applications for benefit of humans. Nanotoxicity of nanoparticles studies extensively by different scientist's around the globe [40-48]. The use of NPs in drug delivery systems might be the future thrust in the field of medicine. NPs are used in the treatment of epilepsy, venereal infections, acnes and leg ulcers. The Green chemistry synthetic route can be employed for both silver and gold silver nanoparticles synthesis. Among the NPs, the biological organisms such as bacteria, fungi and yeast or several plant biomassor plant extracts have been used for nanoparticles synthesis used for a number of applications from electronics and catalysis to biology.

CONCLUSION

The "green" route for nanoparticle (NP) synthesis is of great interest due to eco-friendliness, economic prospects, and feasibility and wide range of applications in nanomedicine, new category catalysis medicine, nano-optoelectronics, etc. It is a new and emerging area of research in the scientific world, where day-by-day developments is noted in warranting a bright future for this field. This green chemistry approach toward the synthesis of NPs and others have many advantages such as, ease with which the process have economic viability, etc. It was concluded that biological mediated synthesis of NPs possesses potential antimicrobial, anticoagulant activity, and anticancer activities. Many reviews have recently considered approaches to investigate the toxicology of nanoparticles and have recognized that preliminary toxicity data can be usefully obtained from *in vitro* studies. The characterization analysis proved that the particle so produced in nano dimensions would be equally effective as that of antibiotics and other drugs in pharmaceutical applications. An improved understanding of the risk factors related to nanomaterials in the human body and the ecosystem will aid future development and exploitation of a variety of nanomaterials. The ongoing research efforts are focussed on evaluating the safety of nanomedicine and formulating the international regulatory guidelines for the same, which is critical for technology advancement. With vast technology push, there are many challenges head that need to be understood and solve in order to make the NP-based products commercially viable. There are some significant gaps in knowledge that need to be addressed. Quantitative data on toxicological effects of nanoparticles are still scarce even at the single organism level. Presently, the researchers are looking into the development of cost-effective procedures for producing reproducible, stable and biocompatible metallic NPs from bioresources.

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