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Mini-review

Green synthesis of silver nanoparticles: An approach to overcome toxicity

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ABSTRACT

Nanotechnology, with its advent, has made deep inroads into therapeutics. It has revolutionized conventional approaches in drug designing and delivery systems by creating a large array of nanoparticles that can pass even through relatively impermeable membranes such as blood brain barrier. Like the two sides of a coin, nanotechnology too has its own share of disadvantages which in this scenario is the toxicology of these nanoparticles. Numerous studies have discussed the toxicity of various nanoparticles and the recent advancements done in the field of nanotechnology is to make it less toxic. "Green synthesis" of nanoparticles is one such approach. The review summarizes the toxicity associated with the nanoparticles and the advancement of "green" nanomaterials to resolve the toxicity issues.

Contents

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1. Introduction

The revolutionary field of nanotechnology has become a major thrust in scientific research. Nanotechnology has adapted itself to various field of science and technology including physics, chemistry, etc. It is expanding and continues to change the way we perceive and execute things and has a pronounced effect on therapeutics and shaping the ever evolving society and influencing our daily lives (Chakraborty et al., 2011).

Nanomedicine has become a leading research field. Scientists are involved in synthesizing safe, effective, and most of all cheaper and less toxic drugs to combat diseases like cancer, epilepsy, etc. These nanoparticles have a site specific action due to which only a safe and a prescribed dosage of drug molecules need to be administered and thus helps in reducing the undesired toxicity. These nanoparticles due to their targeted action increase the efficacy of the drug. Their small size gives them an edge while evading the immune responses and also gives them the ability to cross relatively impermeable membranes (Uchegbu and Schatzlein, 2010).

2. Toxicology of nanoparticles

The flip side of the nanoparticles is its toxicity. The nanoparticles of various origins react differently in administered environments (Kurek et al., 2011). Society of Toxicology defines toxicology as "the study of the adverse effects of chemical, physical, and biological agents on people, animals and the environment".

Toxicity studies generally involve experiments where number of cells and organs are subjected to varied doses of chemicals and their response are taken into account over a period of time. These dose related responses are important because they help in determining the appropriate amount of drug that is to be administered, lethal dose (LD_{50}) and median toxicity (MD_{50}) and the limit of its exposure to prevent any side effects. In traditional toxicological studies via cytotoxic assays, the focus is mainly on soluble chemicals that upon administration exhibit cellular toxicity, whereas in nanoparticles, it is based on the specific sizes, shapes and their density. This causes nanoparticles to aggregate and agglomerate at specific sites in the target cells or organs by diffusing through the membranes leading to a colorimetric result. Hence traditional in vitro assays on nanoparticles lead to misrepresentation of cellular uptake data and the results obtained make them less dependable. The structurally varying nanoparticles are considered important in toxicological studies because of their unique properties, for example, the carbon nanotubes are known for their unusual mechanical and electrical properties. These nanoparticles are considered potentially toxic due to their resemblance to asbestos and carcinogenic fibers; they are also graphitic and are therefore expected to be biologically persistent in the body. Their fibrous structure makes them toxic even in the occupational environment (Nature Nanotech Editorial, 2011). Then there are the magnetic nanoparticles, which are widely used for tracking and tagging of cells in vivo. And also have recently been considered of a therapeutic value in regenerative medicine in the form of SPIONs (superparamagnetic iron oxide) which are coated with dextran to make them biocompatible (Solanki et al., 2008). But, these become toxic if overdosed as they have the ability to aggregate due to their shape and size (Markides et al., 2012).

The in vitro testing methods have revealed the general and biological properties of known materials as they acquire nanoscale structure and result in the formation of nanoparticles, thereby leading to tremendous applications in therapeutics. Nanoparticles can cross membrane barriers through transcytosis, which facilitates the drug to be functionalized onto these nanoparticles using hydrophilic surfactants like Tween-80 for the targeted action (Sun et al., 2004). These studies have also shown that exposure of nanoparticles on cells results in DNA damage, causing cancer and developmental toxicity which further leads to growth retardation, malformation or death in embryos. It is also shown to have provoking oxidative stress and inflammatory responses as they travel along the dendrites and the axons (Durnev, 2007). Toxicology studies showed deleterious effects on people who came in contact with nanoparticles as a result of their occupation, mainly by ultrafine particle inhalation, which is due to its large surface area and its reactivity or intrinsic toxicity (Poma and Di Giorgio, 2008). Numerous in vivo experiments on intravascular or intracavitary drug delivery systems, tumor chemotherapy or antiangiogenic therapy were carried out using nanoparticles with magnetic properties. Experiments conducted on mice have shown nanoparticle aggregates in the brain tissues but no disturbance or apparent toxicity has been observed (Kim et al., 2009). A problem would arise if the magnetic nanoparticle aggregates start corroding after a period of time, which would lead to toxicity in neural tissues causing them to degenerate or cause hemorrhages or tumors. Coating with biocompatible and less toxic copolymers like polyethyleneoxide triblock copolymers of 15 kDa can prevent the aggregation of these magnetic nanoparticles (Hafeli et al., 2009).

Some of the reasons for toxicity are the surface chemistry of nanoparticles and the gap junctions present in the cells that allow transmission of ions and molecules into the cell. The oxidative stress is the result of the free radicals generated from the reactive surface of nanoparticles and the DNA damage by ATP transmission through the gap junctions (Vijayaraghavan et al., 2010). A therapeutic profiling of the nanoparticles is done to measure their toxicity. One such theoretical avenue is the Pre-clinical Safety Assessment (PSA) system that has not been explored practically yet. The existing PSA runs a series of in vivo tests on the administered nanoparticles to determine the toxicity of their chemical properties. Every individual has a different genetic makeup that causes the bioavailability and the kinetics of the drugs to vary from person to person, thereby causing varied impact on the toxicity of the administered nanoparticles (Oberdorster et al., 2005). The defects in the existing PSA system are seen in the documented studies of cytogenetic effects of the chrysolite asbestos fibers and zeolite particles. The routine method is ineffective in determining the genetic defects caused by these particles. Experiments done using larger particles (2–10 μ) have shown similar toxic mechanisms involving oxidative stress and pro-oxidant effects.