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Histopathological Impact of Silver Nanoparticles: A Review

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ABSTRACT

Silver nanoparticles (AgNPs), as the name suggests are the silver particles ranging in nanometers i.e. 1-100 nm. Nano silver has became a blossoming field of study due to its vast consumer products and biomedical applications. The breakneck use of AgNP, due to its antimicrobial activity and distinct physico-chemical properties that are rendered due to its minuscule size , has forced us to raise a concern about the potential toxicity hazards of AgNPs. These can be synthesized using various methods but due to cost effectivity and eco-friendly approach of green synthesised nanoparticles, it has been revolutionised. Very scant insights are present by the previous studies on the toxicity of green AgNPs on aquatic system and on fishes. Thus, in this review we are going to focus on the effect of green synthesized AgNPs on histopathology of freshwater fish *Clarias batrachus*.

Key word: *Silver Nanoparticles, AgNPs, Toxicity, Hematology, Green synthesised*

Introduction

The term nanoparticle is a combination of the words ìnanosî (Greek: dwarf) and ìparticulumî (Latin: particle). In scientific context ìnanosî normally refers to magnitude of 10^{-9} meters. Nanoparticles can be traditionally defined as particles whose at least one dimension is in range of 1-100 nm. But sometimes nanoparticles can exceed the size of 100 nanometer up to 1000 nm. Nanoparticles are dealt in a multidisciplinary field i.e. nanotechnology and it was first proposed by Richard Feynman in 1959 during his well famous lecture "there is plenty of room at the bottom" that is why he is also called father of Nanotechnology. Nanoparticles can synonymously be called Nano crystals or nanomaterials.

The human made nanoparticles can be categorized into- Non-metallic inorganic NPs- TiO_2, SiO_2, ZNO, CaO; Carbon based NPs – Carbon nanotubes (CNTs), Fullerenes etc.; Quantum dots- Carbon Telluride, Cadmium selenide; Quantum dots free of Cadmium; Nano polymers and dendrimers nanotubes Nano rods, Nano cellulose etc.

Since past few decades there have been a Nano revolution leading to rise in manufacturing and application of NPs many folds. This vast use of NPs in many fields is due to the uniqueness of properties that is not shown by bulk material (Auffan *et al*., 2009).

Silver Nanoparticles (AgNPs)

Silver has been used since ages in human history primarily due to its metallic lustre and antimicrobial property. It exhibits remarkably unusual physical properties from its bulk material e.g. more active surface area, better porosity (Alt *et al*., 2004), agglomeration tendency (Wei *et al.*, 2015), surface enhanced Raman scattering, chemical stability, ther-

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mal and electrical conductivity (Capek, 2004). AgNPs have also a very special property, i.e. its excellent antimicrobial activity that can be due to the release of Ag^{+} that can cause harm to DNA. These ions also interact with the thiol groups of some essential enzymes and destroy them (Matsumara *et al.,* 2003).

Many techniques are present for AgNP synthesis e.g., physical methods, chemical, electrochemical methods, microwave assisted methods (Horikoshi *et al.*, 2013). These methods are expensive or use toxic substances hence these are 'not so favored' methods. A more economic and eco friendly method is the biological method also called the green synthesis. In this method, many living organisms can be employed e.g. variety of microorganisms like bacteria, fungi, plants and animals e.g. *Spirulina* (Mohdieh *et al.,* 2012), *Aspergillus niger*, *Fusarium oxysporum* and *Alternaria solani* (Juraifani *et al*., 2015). Animal blood can also be a potential source for AgNP synthesis (Kakakhel *et al.,* 2021). Some of the plants used for AgNPs synthesis are Neem (Namratha and Monica, 2013), Aloe vera (Logaranjan *et al.,* 2006) and many more.

Applications of AgNPs

Left the pathogenic activity this particle is also used in different fields such as in Catheters (Wu *et al.,* 2015), in Cardiovascular implants (Shawcross *et al*., 2017), Face mask (Li *et al*., 2006), Wound dressings (Kalantari *et al*., 2020), in Textiles (Radetic, 2012), Water treatment (Namratha and Monica, 2013), in Nanosensors- (Ravichandran *et al.,* 2021). AgNP can be used as fertilizer pesticide and pesticide carriers (Kale *et al*., 2021), Food Packaging – (Carbone *et al.,* 2016), in treatment of cancer (Kuppusamy *et al.,* 2016 and Parnsamut *et al*., 2014) and the list is very long and hence we can say that AgNP has left no field untouched.

Toxicity of Silver Nanoparticles

AgNPs can be transformed in the environment by oxidation and dissolution, aggregation, sulphidation, chlorination and regeneration (Yu *et al*., 2013). Many studies have now been conducted to assess the toxicity of AgNPs on environment and different organisms also. Silver nanoparticles can elicit many consequences like cell activation, generation of reactive oxygen species (ROS) and cell death. It has been recently found that the mitochondrial functions also decreased in presence of silver nanoparticles (Teodoro *et al*., 2011).

Mazumdar *et al*., (2011) found out that during AgNP penetration in root cells of *Oryza sativa* and damaged the vacuoles as well as the cell wall. When compared the toxicity of AgNPs to Silver ions in *Daphnia magna* and found that AgNP falls under the "category acute1" to *Daphnia* neonates according to GHS (Globally Harmonize System of Classification and Labelling of Chemicals) and hence the release of the same should be carefully monitored (Asghari S. *et al.,* 2012). Greulich *et al.,* (2012) in a research concluded that silver nanoparticles are equally harmful to the bacteria in the same concentration range as to the human cells. Xue *et al.,* (2016) assessed the effect after exposure to AgNP on the proliferation and on the induction of apoptosis in HepG2 cell line of liver cells in different concentration range and found about 10% decrease in cell viability and also observed increase in apoptosis and generation of reactive oxygen species (ROS).

Cha *et al*., (2008) in his study concluded that AgNP exposure revealed vacuolization and hepatic focal necrosis, hyperplasia of bile ducts, increased infiltration of inflammatory cells and central vein dilation. Pandit *et al.,* (2018) in a study concluded that *Clarias batrachus* is more resilient to AgNP toxicity than other fishes. His study also showed many effects of AgNP on *Clarias batrachus* like erratic swimming, jerky movement increase in buccal movement, decrease in rate of feeding, increase in opercular movement etc.

AgNP can also pass the blood brain barrier (BBB) through endothelial cell membrane and can lead to the decreased cell viability especially of neurons. It has also been observed that AgNP may negatively affect proliferation of cerebral cells in human (Coccini *et al.,* 2014). It is also observed that the green synthesized AgNPs are comparatively less toxic. The factors that are responsible for reduction in toxicity of AgNPs depend upon the stabilizers, reducer and coating molecules (Velidandi A. *et al*., 2020). Thus green synthesized AgNPs may be employed for several biomedical applications and for consumers commodities also.

Rajkumar *et al*., (2015) experiment on *Labeo rohita* concluded that silver and a particles treated fishes should proliferation of brachial chloride cells which results in lamella fusion and formation of aneurism which increases the risk of rupture and hemorrhage and may lead to even death. (Kakakhel *et al*., 2021; Shukla *et al.,* 2017). Joo *et al*., 2016 in a study showed that when silver nanoparticle exposed fishes were kept in different salinities they exhibited different extent of histological changes e.g. when fishes were kept in low salinity they showed hypertrophy, lamellar fusion, clubbing, hyperplasia, in addition to these changes when exposed to moderate and higher salinities necrosis and aneurism were also observed, this suggests that change in salinity can result in change in the level of toxicity.

Increase in silver nanoparticle concentration can lead to severe histopathological abnormalities in organisms (Mabrouk *et al*., 2021), his study revealed that when fishes were exposed to low silver nanoparticles concentration (10 mgl-1) they showed better growth performance, feed utilization and nonspecific immune response when challenged with *A. hydrophilia*. But when AgNP concentration is increased then the total bacterial count is decreased in dose dependent manner, but it also affected negatively on the growth performance and other physiological phenomenon of fishes, suggesting the potentiality of silver nanoparticle toxicity.

Abirami *et al*., (2017) in his study assessed the effect of green synthesized silver nanoparticles and found alterations in the gill structure with degeneration of primary gill lamella, hyperplasia, necrosis and fused primary lamella. Furthermore vacuolisation, necrosis was also observed in liver tissues, somewhat similar results were also reported by Abarghoei *et al*., 2016.

In a study by Naguib *et al.,* (2020) on *Clarius garienpinus* indicated several changes when exposed to AgNPs e.g. rise in serum glucose and serum total lipids and a decrease in serum total protein, albumin and globulin and also indicated that exposure to silver nanoparticle at lower concentration caused deduction in cell size, infiltration of inflammatory cells in blood vessels and areas of hepatic necrosis etc.

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