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RESEARCH ARTICLE

Nanotoxicological Effects of Silver Nanoparticles

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ABSTRACT

Nanotechnology is a branch which connects every corner of science. The chemistry of biological system can also be altered by introducing the synthesized nanoparticles. Characteristics of any material in Nano range change its property. They can easily reach inside the sensitive mammalian cells of liver, lung, brain by the means of inhalation or injection and due to the larger surface area of the nanoparticles the cellular interaction in easy to achieve. The studied nanoparticles were analyzed upon fibroblasts and macrophages whereas, they were tested upon human PC3 epithelial cells also but they all didn't show a similar pattern. Surface modification has also been done with various compounds such as metelates which says that the properties of nanoparticles can be enhances but they might be having some adverse effects. These particles possess the ability to deliver the drugs and can heal the wounds but the generation of unusual toxic compounds within the cells makes it less possible. Studies on bacterial and human cells illustrate some diverse behaviors of nanoparticles. The cellular reactions in which these particles take part in may affect up to the genetic level. The modified surface of nanoparticles holds them towards stability however silver being a noble metal causes damageable effects which draws attention to study.

Key words: *Nanoparticles, Nanotechnology, Reactive Oxygen Species*

INTRODUCTION

Particles in their nano range exhibit distinct properties in biological environment. Silver nanoparticles (AgNPs) are intensively being used as antimicrobial agents and drug carriers in biomedical fields. In-vitro and in-vivo studies of any micro-organism or living cell showed the anonymous characteristics of silver. The inert nature of silver promotes to get into several reactions but after every interaction in such range with cells happens, the cells gets adversely affected but so on the anti-bacterial effect of silver holds it to perform many useful results. Silver nanoparticles are usually toxic to the cells and many times it requires a vector molecule to get stable. Molecules must be specifically chosen in context with silver as an inorganic compounds or alloys depending upon the targeted cell. It has also be reported as AgNPs in association with other elements shown more bacterial mortality rate than AgNPs alone as in the formation of bacterial colonies or biofilms around wounded soft and hard tissue leads to the infection but when treated with associated AgNPs, the results were considerable. Furthermore, statistical data were analyzed, which shows both toxic as well as antimicrobial nature of silver nanoparticles.

RESULTS AND DISCUSSION

Studies on nanoparticles has been done on both gram positive as well as on gram negative bacteria which shows resemblance in some properties for instance nanoparticle size, surface area and surface corona are the major influencing factors that affects cellular metabolism and toxicity. One of the major causes of AgNPs that it stimulates the production of ROS and thus damages the DNA. In a study, it was reported that AgNPs cause more toxicity than Ag in its ionic form (MargrietPark*, et al,.* 2011). Studies on L929 fibroblast cells and RAW 264.7 macrophages show an unusual toxicity pattern, it says the silver nanoparticles cause toxicity in dose and size

dependent manner. The smaller the nanoparticle the more toxic response is generated due to the easier uptake. In contrast with those two cells used they both got affected at different concentration as fibroblast get effected easily whereas macrophages making the particles neutralized by its functionalized membrane but at higher concentration they also responded the same. Though silver nanoparticles show their adverse effect, result into the decrease in metabolic activity of the cell. In addition to embryonic stem cell differentiation they were again found out to be cytotoxic. Similar studies also exhibit that the toxicity may be caused due to the release of the surface ion from the respective AgNPs because of the larger surface area of smaller nanoparticles (Park, *et al*,. 2010). Presence of the particles in the cells disturbed its anatomy. The inability of electron that is present in complex IV of mitochondria, to bind with derivatives of oxygen and thus forming reactive oxygen species and oxidative stress, causing cytotoxicity. But the effects is not yet restricted to cytoplasmic levels, damaging DNA which ultimately leads to cell cycle arrest at G_2/M phase of cell division and cell death. Starch, quercetin and various other materials has been used to make these particles compatible within the biological environment. A comparative study on fibroblast and glioblastoma cell has also being reported (AshaRani, *et al,. 2009*), in which silver nanoparticles were used with starch coated upon it. According to it, in the presence of nanoparticles cells was not affected till 24h but start affecting from 48h to 72h where interestingly ATP concentrations were found out to be dropped drastically. Nanoparticles formed clusters and so after a considerable time the decrease in ATP depletion is noticed hence, silver nanoparticles did metabolic arrest i.e. on low ATP levels. But when starch alone used, no significant effect is observed showing the biocompatible nature of starch. Mitochondria have been reported again as the major site of ROS production in cell. A possible mechanism of the generation ROS stated as when the Ag^+ ion binds to the membrane protein it causes the leakage of positive ions into the cell. Inside the cell the Ag^+ ion binds to the enzymes of bacterial respirator chain which in turns prevents the electrons to reach oxygen and thus generating reactive oxygen species. Proteomic analysis showed the reduction in ribosomal subunit S2, maltose transporter and succinyl Co-A synthetase which caused the low levels of ATP (Hara, *et al*,. 2005). Reduced content of ribosomal subunit, succinyl and maltose transporter made the reduction of protein, reduction in ATP respectively which leads to cell death. The cellular antioxidant level goes down with the simultaneous generation of ROS and thus it is stated that antioxidants, certain enzymes and methods can turn down the production of ROS. Subsequent studies have shown that two specific organs i.e. liver and lungs were most affected by the prolonged exposure of AgNPs (Takenaka, *et al,.* 2001 and Sung, *et al*,. 2008). Silver nanoparticles are also known to be cytotoxic at non-cytotoxic doses, as in a study on human mesenchymal cells reports the unsafe behavior (Greulich, *et al,.* 2009). On the other hand, AgNPs in association with other compounds such as TiO_2, show high photocatalytic activity. 5-10% failure of peri-implantitis is still faced with many dental implants, the implants thereby causes the biofilm production in the near tissue. The Bacteria *Streptococcussanguinis*is found as the causative agent (Besinis*, et al*,. 2017). By using silver nanoparticles in accordance with the photocatalytic agent and hydroxyapatite (biocompatible ceramic nanomaterial) it enhances the bacterial mortality up to 100% whereas, it was also reported that the combination of TiO_2 with Ag sometimes produced radicals. Surface modification of the nanoparticles has also been showed quite an impressing behavior. Many compounds are being used on the surfaces to enhance their stability and ability.(Daima, *et al,.* 2014) POMs (polyoxometalates) a 3D structure which has a good antibacterial, antitumor, antiviral properties but they are not much stable and their stability is maintained by some amino acids i.e. tyrosine. They are caged structures having the metal ions in its high oxidation state shared with oxygen or phosphorous. POMs are usually made up from transition metals. The functionalized surface corona with POMs and AAs now show better bacterial mortality rate on both gram-positive and gram-negative bacteria but some adverse effects came in front, as due to the presence of silver the di-sulphide bonds is affected, the metabolism and the iron homeostasis in the bacterial cell is disturbed badly thus, leaded to the production of ROS (an irreversible damage). Interestingly, human PC3 epithelial cells does not get affected with the same experiment as the data says, over up to 5 times the concentration of silver nanoparticles into the cell, cell responded normally, hence no toxicity in the cell

reported (Chandrana, *et al*,. 2017). Instead the synthesized NPs should be non-toxic and the surface factionalized corona should be minimalized to reduce or to reform the formation of unnecessary toxic compounds in the cell and hence making them a better option to uptake.

CONCLUSION

The studied responses and certain other reports showed that silver nanoparticles impart a very effective property and though have capability to interact with the cells very efficiently. But the caused toxicity within the cell is so severe that in some cases the observed death of cell occurred in micro seconds. No such methods have been thus reported to prevent the production of oxidative stress. In-case if these nanoparticles achieve the ability to perform well in the biological systems, the affected cells can be cured very effectively using these particles. And further they can also help in treating cancer cells in a controlled method.

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