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Biologically Synthesised Silver Nanoparticles Induces Autophagy and JNK Signaling as a Pro-Survival Response by Abrogating Reactive Oxygen Species Accumulation in Cancer Cells

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Abstract : Metal nanoparticles in recent years have gained importance in cancer therapy due to their enhanced permeability retention effect. Among various nanomaterials, silver nanoparticles (AgNPs) have received considerable attention due to their unique properties like conductivity, chemical stability, relative lower toxicity and outstanding therapeutic potential, such as anti-inflammatory, antimicrobial and anti-cancerous activities. In this study, we took a greener approach to synthesize silver nanoparticle from fungus and analyze its effects on both epithelial and mesenchymal derived cancer cells. Much research has been done on nanoparticle-induced apoptosis, but little is known about its role in autophagy. In our study, the silver nanoparticles were seen to induce autophagy which was analyzed by studying the expression of several autophagy markers like, LC3B-II and ATG genes. Monodansylcadaverine (MDC) assay also revealed the induction of autophagy upon treatment with AgNPs. Inhibition of autophagy by chloroquine resulted in increased cell death suggesting autophagy as a survival strategy adopted by the cells. In parallel to autophagy induction, silver nanoparticles induced ROS accumulation. Interestingly, autophagy inhibition by chloroquine increased ROS level, resulting in enhanced cell death. We further analyzed MAPK signaling upon AgNP treatment. It was observed that along with autophagy, activation of JNK signaling served as pro-survival while ERK signaling served as a pro-death signal. Our results provide valuable insights into the role of autophagy upon AgNP exposure and provide cues to probabilistic strategies to effectively sensitize cancer cells.

Keywords : autophagy, JNK signalling, reactive oxygen species, silver nanoparticles
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