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Induction of Apoptosis in Cancer Cells at Low Silver Nanoparticle Concentrations using Chitosan Nanocarrier

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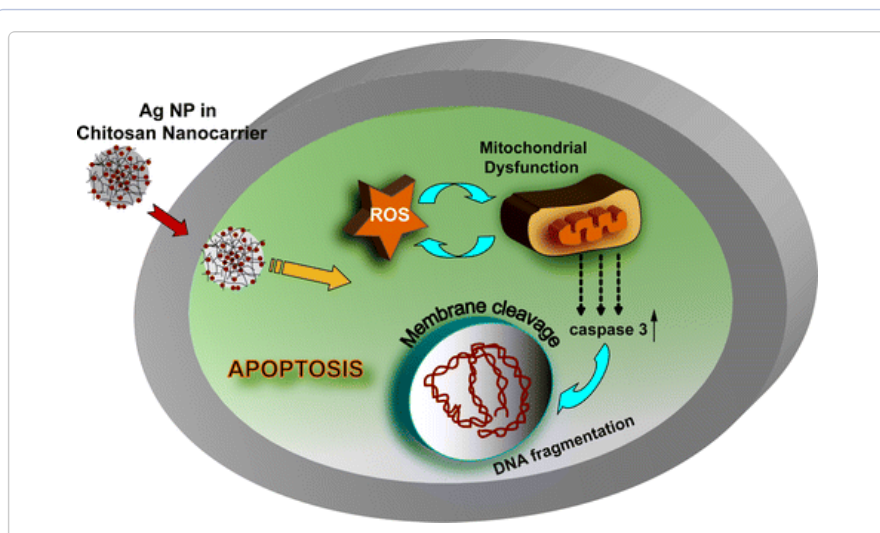
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Abstract



We report the development of a chitosan nanocarrier (NC)-based delivery of silver nanoparticles (Ag NPs) to mammalian cells for induction of apoptosis at very low concentrations of the NPs. The cytotoxic efficacy of the Ag NP-nanocarrier (Ag-CS NC) system in human colon cancer cells (HT 29) was examined by morphological analyses and biochemical assays. Cell viability assay demonstrated that the concentration of Ag NPs required to reduce the viability of HT 29 cells by 50% was $0.33 \mu\text{g mL}^{-1}$, much less than in previously reported data. The efficient induction of apoptosis by Ag-CS NCs was confirmed by flow cytometry. Additionally, the characteristic nuclear and

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morphological changes during apoptotic cell death were investigated by fluorescence and scanning electron microscopy (SEM), respectively. The involvement of mitochondrial pathway of cell death in the Ag-CS NCs induced apoptosis was evident from the depolarization of mitochondrial membrane potential ($\Delta\Psi_m$). Real time quantitative RT-PCR analysis demonstrated the up-regulation of caspase 3 expression which was further reflected in the formation of oligo-nucleosomal DNA "ladders" in Ag-CS NCs treated cells, indicating the important role of caspases in the present apoptotic process. The increased production of intracellular ROS due to Ag-CS NCs treatment indicated that the oxidative stress could augment the induction of apoptosis in HT 29 cells in addition to classical caspase signaling pathway. The use of significantly low concentration of Ag NPs impregnated in chitosan nanocarrier is a much superior approach in comparison to the use of free Ag NPs in cancer therapy.

Keywords (keywords): [silver nanoparticle](#); [chitosan nanocarrier](#); [apoptosis](#); [mitochondrial membrane potential](#); [reactive oxygen species](#)

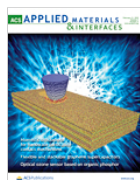
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Sachin Kumar, Shammy Raj, Elayaraja Kolanthai, A.K. Sood, S. Sampath, and Kaushik Chatterjee

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