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Bioengineering of green-synthesized TAT peptide-functionalized silver nanoparticles for apoptotic cell-death mediated therapy of breast adenocarcinoma

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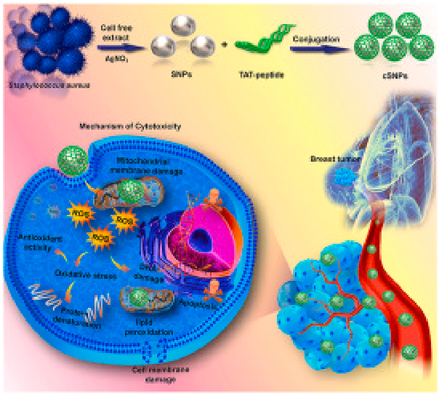
Highlights

- Silver nanoparticles (SNPs) were successfully fabricated from *Staphylococcus aureus* cell-free extract.
- Surface modification of SNPs was executed by conjugating trans-activator of transcription (TAT) peptide.
- TAT peptide-conjugation enhanced the induction of apoptosis in the breast adenocarcinoma cells.
- Conjugated SNPs exhibited potential cytotoxic activity of IC50 (25 µg/mL) against MDA-MB-231 breast cancer cells.
- Surface functionalization of SNPs by human-derived peptides could be a new and promising approach in cancer therapy.

Abstract

Green synthesized silver-nanomaterial has exhibited significant advantages as cancer therapeutics due to their exclusive characteristics that cause inducing various forms of cell death; particularly, they have attracted much attention in the treatment of breast cancer. More specifically, the exploration of silver nanoparticles (SNPs) in investigation of cancer treatment is of booming interest due to the opportunity to customize the physicochemical properties of NPs, to enhance their biocompatibility and interactive potentials through surface functionalization. In the present study, first SNPs were fabricated from Staphylococcus aureus cell-free extract, and then the surface modification was executed by conjugating trans-activator of transcription (TAT) peptide, which is a cellpenetrating peptide to enhance the induction of apoptosis in the breast adenocarcinoma cells. The physicochemical characteristics of both virgin SNPs and TAT peptide conjugated SNPs (cSNPs) were evaluated using UV–vis spectrophotometer, FTIR, SEM-EDX, TGA, DSC, and TEM. FTIR analysis revealed the involvement of amide and amines in SNPs synthesis. The SEM analysis confirmed the spherical shape of SNPs, while EDX showed the elemental nature of silver. TGA determined the protein loss at second weight loss of nearly 45%, and DSC confirmed the endothermic phase transition of both SNPs and cSNPs. Moreover, TEM revealed the particle size of about 26.94 nm and 21.94 nm for SNPs and cSNPs, respectively. In regard to the cancer therapeutic potentials of NPs, the cSNPs exhibited potential cytotoxic activity of IC50 (30.05 μg/mL) against MDA-MB-231 breast cancer cells compared to SNPs that induced apoptosis by enhancing the upregulation of p53 protein expression. Internment flow cytometry data confirmed the productions of ROS radicals in the treated cells of the MDA-MB-231 cells. Overall, our study shows that the surface functionalization of SNPs by employing potential inhouse human-derived peptides could be a new and promising approach in cancer therapy.

Graphical abstract



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Introduction

Nanotechnology is contemplated as converging proficiency of materials science, physics, chemistry, and biology, because of its plethora of structural uniformity and its great performance in every field of science [[1], [2]]. Nanoparticles (NPs) are gaining the utmost attraction of research among scientists due to their unique characteristics and a relatively large number of applications in biomedicine like drug delivery, vaccines, cancer therapy, regenerative medicine, etc. [[3], [4], [5]]. Besides these activities, cellular uptake and toxicity are the major concerns while using NPs in biomedical applications [[6], [7]]. In addition, the biocompatibility and the capability of specific internalization by the target cells and its discrimination from non-target cells is a challenging issue during the final applications [8]. Moreover, the surface functionalization of NPs embroils a course that intends to enhance and/or enumerate unique characteristics that are useful in biomedicine applications [9]. However, various nanomaterials have multi-intensified distinct chemical properties and functional groups defined on their surface to be utilized in the preliminary functionalization step [10].

Silver comes in several forms, including silver ions, silver oxide, and silver nanoparticles. Silver oxide nanoparticles with two atoms are extremely hazardous to a wide range of bacterial infections, and silver oxide nanoparticles are employed to detect the highly polluting chemical 4-nitrotoluene. (4-NT) [11]. Silver ions include silver atoms with one electron and are harmful to bacteria cells; however, their potency fades quickly and all ions cannot reach the dermis layer. However, silver nanoparticles contain hundreds to thousands of silver atoms in a small crystal and can kill the bacterials pathogens for a long time and quickly penetrate the dermis. Biofabricated silver nanoparticles were found to be extremely hazardous to both gram positive and gram negative bacterial