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Bioengineered silver nanoparticles induced apoptosis through upregulation of caspase 3 and caspase 8 proteins in breast adenocarcinoma MDA-MB-231 cells and impede angiogenesis

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Highlights

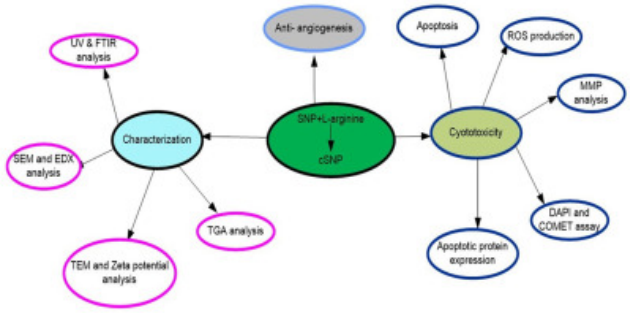
- Silver nanoparticles (SNP) were synthesized from *M.lunu-ankenda* and conjugated with L arginine (cSNP).
- CSNP were verified by various microscopic examinations.
- CSNP displayed good toxicity towards breast cancer cells.
- ROS production and mitochondrial membrane depolarization caused apoptosis.
- CSNP induces significant DNA damage, upregulates caspase 3 and caspase 8 apoptotic proteins and showed excellent anti-angiogenesis characteristics.

Abstract

In recent years, a lot of research has been done on silver nanoparticles (SNP) due to their numerous applications in the biomedical, pharmaceutical, and drug delivery industries. In this present study SNP were green synthesized using *Melicope lunu-ankenda* (*M.lunu-ankenda*) leaf extract. The addition of $AgNO_3$ causes a color change. L-arginine addition results in further colour changes confirming conjugation. A UV–Vis spectrophotometric examination showed that the absorption peak for SNP was 435 nm, while the peak for L-arginine SNP (cSNP) was 422 nm. FTIR

analysis confirmed the association of amides and amines with nanoparticles. The spherical nature of the silver was disclosed by SEM, and its elemental character is verified by EDS. The thermal stability of the nanoparticles is determined by TGA analysis, while TEM examination verifies their spherical shape. Using the MTT assay, these cSNP exhibited outstanding toxicity analysis (IC_{50} 38.72 µg/ml) against MDA-MB-231 cells. These cSNP causes damage to the mitochondria (JC1 staining), which causes oxidative stress and the production of ROS with 83% of DCF expression in cancer cells. Furthermore, as demonstrated by the Comet assay and DAPI, these cSNP cause good DNA damage in the treated cells. Additionally, using flow cytometry, cSNPs potentially trigger apoptosis by triggering the expression of caspase 3 and caspase 8 proteins. Additionally, through CAM, cSNP demonstrated strong anti-angiogenesis activity by reducing the number of blood vessel branches. These findings suggest that cSNP may be crucial for drug delivery and cancer treatment.

Graphical abstract



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Introduction

Breast cancer remains a major health issue, ranking as the most prevalent form of cancer among women and a primary cause of cancer-related fatality on a global scale. The disease is intricate and diverse, exhibiting a range of subtypes and molecular traits that impact both its course and reaction to therapeutic interventions (Orrantia-Borunda et al., 2022). Treatment for breast cancer is multimodal and includes systemic medicines such as immunotherapy, chemotherapy, endocrine therapy, and anti-HER2 therapy in addition to surgery and radiation (Harbeck et al., 2019). Research on treatments has been looking into different ways to create medications that are safe for people to take and that are also effective against cancer cells.

Silver nanoparticle (SNP) capitalizes on the increased permeability and retention impact of tumor microenvironments to provide targeted medication delivery to tumors. This could result in less systemic toxicity and more efficacy (Tiwari et al., 2023). Because of their precision targeting, stability, and biocompatibility, nanoparticles can address the drawbacks of conventional treatments, including non-specificity and multi-drug resistance (Gavas et al., 2021). Due to its lack of specificity, the previous cancer treatment had negative effects on both cancer cells and healthy tissues. On the other hand, drugs can be selectively delivered to cancer cells using nanoparticles without endangering healthy organs. This targeted strategy lowers the possibility of side effects, lowers the danger of harm to neighboring tissues, and improves therapy, efficacy and overall safety. Furthermore, it has been demonstrated that SNP causes cancer cells to undergo apoptosis by triggering the enzymes caspase, which is essential for carrying out apoptosis, and producing reactive oxygen species (ROS). This points to a mechanism by which SNP prevents cancer (Yuan et al., 2018). Furthermore, it has been discovered that combining SNP with other anticancer drugs, increases cytotoxicity in cancer cells, providing a synergistic method of cancer treatment (Ullah et al., 2020a; Yuan et al., 2018).