



Transactivator of transcription peptide conjugated copper oxide nanoparticles: A nano-warrior against breast cancer - Insights from biosynthesis, characterization, and cellular studies

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Received 25 June 2023, Revised 12 September 2023, Accepted 18 September 2023, Available online 26 September 2023, Version of Record 1 October 2023.

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<https://doi.org/10.1016/j.jddst.2023.104979> 

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Abstract

Nanobiotechnology presents novel opportunities for the treatment of diverse forms of cancer at the nanoscale, exhibiting an outstanding level of effectiveness. Copper oxide nanoparticles (CuONPs) possess notable antibacterial and cytotoxic characteristics. Hence, the primary objective of this investigation is to examine the biomedical utilities of CuONPs that are conjugated with Transactivators of transcription (TAT) peptide. The study further intends to assess the viability of utilizing these conjugated copper oxide nanoparticles (cCuONPs) as an anticancer therapeutic agent for breast cancer treatment. The biosynthesis of CuONPs was effectively achieved using the aqueous extract of Aspergillus assiutensis through the extracellular reduction of 5 mM copper sulphate. The CuONPs that were synthesised underwent conjugation with TAT-peptide, resulting in the formation of cCuONPs followed by its characterization using a range of instrumentation techniques, including UV-visible spectrophotometry, Fourier-transform infrared spectroscopy (FTIR), thermogravimetric analysis (TGA), differential scanning calorimetry (DSC), scanning electron microscopy (SEM), energy-dispersive X-ray spectroscopy (EDX), and transmission electron microscopy (TEM). The nanoparticles exhibited a size range of 2.53–15 nm and possessed a spherical morphology. The MTT assay resulted with the IC₅₀ of 58.34 µg/mL for MDA-MB 231 breast cancer cells and 310.54 µg/mL for normal MCF 10 A cells using cCuONPs. The examination of apoptosis has unveiled various cellular phenomena, including cell condensation, blebbing, and alterations in cell morphology. The cCuONPs were found to induce cell cycle arrest at the S phase with a percentage of 4.46%, while the G2/M phases exhibited a higher arrest rate of 35.44%. The assessment of the mitochondrial membrane potential assay demonstrated a membrane depolarization of 57.45%. The H2DCFDA method demonstrated a 42.75% production of reactive oxygen species (ROS). The application of qualitative reverse transcription (qRT-PCR) demonstrated an observed increase in the expression levels of *IRE-1 alpha*, XBP1, *PERK*, *CHOP*, and *ATF6* genes associated with endoplasmic reticulum stress in the cells treated with cCuONPs, as compared to the group that did not receive treatment. Subsequent examination has demonstrated that the suppression of the epithelial-mesenchymal transition (EMT) pathway effectively hinders the migration and invasion of tumours. Nevertheless, our study additionally demonstrated the upregulation of the p53 and caspase 3 pathway, which serves as the primary mechanism responsible for the initiation of apoptosis in the cancer cells subjected to treatment. Hence, it can be inferred that the cCuONPs possess inherent cytotoxicity against cancer cells, thereby offering significant prospects for the development of nanotherapeutics aimed at effectively targeting breast cancer cells.

Graphical abstract