

## **In vitro Comparison Study of Biologically Synthesized Copper-Disulfiram Nanoparticles with Its Free Corresponding Complex as Therapeutic Approach for Breast and Liver Cancer**

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**Abstract :** The search for reliable, effective, and safe nanoparticles (NPs) as a treatment for cancer is a pressing priority. In this study, Cu-NPs were fabricated by *Streptomyces cyaneofuscatus* through simultaneous bioreduction strategy of copper nitrate salt. The as-prepared Cu-NPs subjected to structural analysis; energy-dispersive X-ray spectroscopy, elemental mapping, X-ray diffraction, transmission electron microscopy, and  $\zeta$ -potential. These biological synthesized Cu-NPs were mixed with disulfiram (DS), forming a nanocomplex of Cu-DS with a size of ~135 nm. The prepared nanocomplex (nanoCu-DS) exhibited higher anticancer activity than that of free complex of DS-Cu, Cu-NPs, and DS alone. This was illustrated by the lowest IC50 of nanoCu-DS (< 4  $\mu$ M) against human breast and liver cancer cell lines comparing with DS-Cu, Cu-NPs, and DS (~8, 22.98-33.51 and 11.95-14.86, respectively). Moreover, flow cytometric analysis confirmed that higher apoptosis percentage range of nanoCu-DS-treated in MDA-MB 231, MCF-7, Huh-7, and HepG-2 cells (51.24-65.28%) than free complex of Cu-DS (< 4.5%). Regarding inhibition potency of liver and breast cancer cell migration, no significant difference was recorded between free and nanocomplex. Furthermore, nanoCu-DS suppressed gene expression of  $\beta$ -catenine, Akt, and NF- $\kappa$ B and upregulated p53 expression (> 3, >15, > 5 and  $\geq$  3 folds, respectively) more efficiently than free complex (all ~ 1 fold) in MDA-MB 231 and Huh-7 cells. Our finding proved this prepared nano complex has a powerful anticancer activity relative to free complex, thereby offering a promising cancer treatment.

**Keywords :** biologically prepared Cu-NPs, breast cancer cell lines, liver cancer cell lines, nanoCu- disulfiram

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