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# Synergistic Effect of Plasma Modified Curcumin and Nano-Doxorubicin in Breast Cancer Cells

Marjan Mohamadali<sup>1\*</sup>, Mostafa Ghanei<sup>2</sup>, Seyed Mohammad Atyabi<sup>1</sup>, Shadab Bagheri Khoulenjani<sup>3</sup>, Shiva Irani<sup>1,2</sup>

<sup>1</sup>Department of Nanobiotechnology, Pasteur Institute of Iran, Tehran, Iran

<sup>2</sup>Department of Biology, SR.C., Islamic Azad University, Tehran, Iran

<sup>3</sup>Polymer and Color Engineering Department, Amirkabir University of Technology (Tehran Polytechnic), Tehran, Iran

## ABSTRACT

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**Introduction:** Doxorubicin (DOX) is a widely used chemotherapeutic agent for breast cancer. However, its clinical utility is often limited due to severe side effects and the development of resistance. Curcumin (CUR), a natural polyphenol, has demonstrated anticancer activities. This study aimed to inhibit breast cancer (BC) cell growth using a combination therapy of cold plasma-modified nano-CUR and nano-DOX in BC cells.

**Materials and Methods:** To enhance the hydrophilicity of CUR, cold atmospheric plasma (CAP) modification was performed. The cytotoxic effects of carboxymethyl chitosan (CMC) nanoparticles loaded with plasma-modified CUR and DOX were evaluated on MCF-7 BC cells and L929 fibroblast cells using the MTT assay. Apoptosis was assessed through the Annexin V assay, and real-time PCR was employed to analyze the expression levels of the *TP53* and *BAX* genes.

**Results and Discussion:** CAP significantly increased the solubility of CUR ( $p < 0.05$ ). The combination therapy of nano-CUR and nano-DOX significantly inhibited cell proliferation ( $p < 0.05$ ). The effective dose of plasma-treated nano-CUR in combination with nano-DOX was lower than that of free CUR and free DOX ( $p < 0.05$ ). This combination therapy resulted in a marked increase in the level of apoptosis (up to 61%) and significantly upregulated the expression of the *P53* and *BAX* genes in MCF-7 cells ( $p < 0.05$ ), indicating an enhanced induction of programmed cell death.

**Conclusion:** The CMC-based co-delivery system of plasma-treated nano-CUR and nano-DOX demonstrated synergistic anticancer activity at reduced effective doses. This combined nanotherapeutic system could serve as a promising candidate for the treatment of BC.



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**Keywords:** Breast cancer, Carboxymethyl chitosan, Cold atmospheric plasma, Nano-doxorubicin

**Corresponding Author:** Marjan Mohamadali

Department of NanoBiotechnology, Pasteur Institute of Iran, Tehran, Iran; E-mail: Marjan.Mohamadali@gmail.com



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