**Combined Effect of Cold Atmospheric Plasma and Curcumin in Melanoma Cancer**

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Curcumin (CUR) has interesting properties to cure cancer. Cold atmospheric plasma (CAP) is also an emerging biomedical technique that has great potential for cancer treatment. Therefore, the combined effect of CAP and CUR on inducing cytotoxicity and apoptosis of melanoma cancer cells might be promising. Here, we investigated the combined effects of CAP and CUR on cytotoxicity and apoptosis in B16-F10 melanoma cancer cells compared to L929 normal cells using MTT method, acridine orange/ethidium bromide fluorescence microscopic assay, and Annexin V/PI flow cytometry. In addition, the activation of apoptosis pathways was evaluated using BCL2, BAX, and Caspase-3 (CASP3) gene expression and ratio of BAX to BCL2 (BAX/BCL2). Finally, in silico study was performed to suggest the molecular mechanism of this combination therapy on melanoma cancer. Results showed that although combination therapy with CUR and CAP has cytotoxic and apoptotic effects on cancer cells, it did not improve apoptosis rate in melanoma B16-F10 cancer cells compared to monotherapy with CAP or CUR. In addition, evaluation of gene expression in cancer cell line confirmed that CUR and CAP concomitant treatment did not enhance the expression of apoptotic genes. In silico analysis of docked model suggested that CUR blocks aquaporin- (AQP-) 1 channel and prevents penetration of CAP-induced ROS into the cells. In conclusion, combination therapy with CAP and CUR does not improve the anticancer effect of each alone.