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Title of thesis: Comparison of the effects of Temozolomide and Acetylshikonin combination therapy with Temozolomide on U-87MG glioblastoma multiforme cells

Summary:

Introduction: Glioblastoma multiforme(GBM) is the most common and aggressive type of glioma, among the brain tumors. The annual prevalence of the disease is less than 10 per 100,000 people in the world and 2-3 per 100,000 people in Iran. Considering its poor prognosis and the patients' short life expectancy, finding an effective treatment sounds extremely necessary. The aim of this study was investigation of the combined treatment of temozolomide, the most common GBM chemotherapy drug, with acetylshikonin as the most effective derivative of shikonin, in inhibition of GBM cells proliferation through induction of the apoptosis.

Methods: U-87MG cell line was selected from GBM cells and the cytotoxic effects of TMZ and ASH were investigated on cells. After obtaining the appropriate concentration for combination therapy, Annexin V/PI staining, the cell cycle pattern, caspase 3/7 activity, intracellular ROS levels and mitochondrial membrane potential were considered.

Results: The treatment of cells with all the two drugs showed a significant decrease in the cell viability. Annexin V/PI staining revealed an increase in the percentage of apoptotic cells. Cell cycle assay showed the increased Sub-G1 population in response to the treatments. A significant increase in caspase 3/7 activity and ROS levels, as well as a decrease in mitochondrial membrane potential, were also observed. These trends were significantly higher in combination therapy to single treatments.

Conclusion: GBM cells combination therapy with TMZ+ ASH, significantly increased the apoptotic cell death compared to TMZ or ASH alone.

Keywords: Glioblastoma Multiforme, Temozolomide, Acetylshikonin, Apoptosis, Combination Therapy