GLIOBLASTOMA AND SELENIUM: POTENTIAL ANTITUMOR EFFECTS OF DIPHENYL DISELENIDE AND TEMOZOLOMIDE

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INTRODUCTION: Glioblastoma (GBM) is a highly malignant and lethal brain tumor, ranked as the most common central nervous system neoplasm worldwide. Temozolomide (TMZ) is the standard first-line chemotherapy for glioblastoma (GBM). Since resistance mechanisms against TMZ have been reported in some gliomas, the search for new drugs are urgently needed to complement or enhance existing therapies that fight GBM. Organic compounds containing selenium, such as diphenyl diselenide (DPDS), have been shown to have antiviral, antioxidant, anti-inflammatory, and antitumor effects in several studies with different experimental models. Still, few studies investigate the antitumor capacity of organoselenium compounds against GBM. OBJECTIVE: Here, we aim to evaluate the antitumor capacity of DPDS as adjuvant therapy to low-dose TMZ (100 μM) in human GBM cell line (U87-MG). MATERIALS AND METHODS: Determination of cellular toxicity and viability of the compounds was performed by 3-(4,5-dimethylthiazol2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay in U87-MG. To assess cell density and determine the effects of DPDS and TMZ exposure on cell survival, we utilized the sulforhodamine B (SRB) assay. To verify the migration of GBM cells after exposure to target compounds, we used the would healing assay. RESULTS: DPDS was evaluated in two different concentrations (10μM and 20μM). DPDS decreased U87-MG cell viability by MTT assay only at 20 μM ($p<0.05$), did not show a synergistic effect with TMZ. In the cell density assay, the co-exposure of DPDS in both concentrations with TMZ reduced the cell density in relation to the vehicle control group (DMSO) (<0.0001) and in comparison to the groups treated only with DPDS or TMZ ($p<0,05$). Regarding cell mobilization, we also verified an inhibition of cell proliferation in the groups co-exposed with DPDS and TMZ ($p<0.05$). CONCLUSION: Therefore, these results indicate that co-exposure to DPDS and TMZ has high antiproliferative and antimobilization capacity in cancer cells, possibly sensitizing the cells to TMZ. The data reinforce the potential of the combined use of DPDS and TMZ as a therapeutic approach for glioblastoma, however additional research is needed to validate its mechanism of action.

Keywords: Glioblastoma; Diphenyl Diselenide; Temozolomide; Selenium; Synergism

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