3rd Brazil-France Symposium on Medicinal Chemistry
Maceió/AL | November 12 -14, 2024

EVALUATION OF THE ACTIVITY OF ANTITUMORAL PROTOTYPES *IN VITRO* IN HUMAN GLIOBLASTOMA CELLS (GM02).

Vitoria de Melo Batista (PG),[1] Andressa Letícia Lopes da Silva (Res)*,[1] Kamily Gyovana Gomes Ferreira (G),[1] Érica Erlanny da Silva Rodrigues (Res),[1] João Kaycke Sarmento da Silva (PG),[1] João Xavier de Araújo Júnior (Prof),[1] Aline Cavalcanti de Queiroz (Prof), [1] Magna Suzana Alexandre Moreira (Prof).

vitoria.batista@icf.ufal.br;

[1] *Universidade Federal de Alagoas*

Keywords: cancer, synthetic compounds; guanylhydrazones; antitumoral activity.

ABSTRACT

Cancer has a high impact on public health and is among the leading causes of death worldwide. Among the various types of cancer, gliomas are considered one of the most aggressive tumors of the Central Nervous System (CNS). They have a high mortality rate, which is associated with genetic mutations that make the search for new drugs essential. Thus, glioblastoma is the most common type of primary CNS tumor in adults and has no curative therapy. Based on these difficulties, the search for specific prototypes is necessary. The present study aims to evaluate the *in vitro* antitumor activity based on the results of guanylhydrazones, whose antitumor activity has already been described in the literature, in cells of a human glioblastoma cell line. In this context, since guanylhydrazones represent a promising class of substances with widely reported tumor-fighting effects, the cytotoxic effect of guanylhydrazones against monocytes and lymphocytes was evaluated through the MTT assay at concentrations of 0.1, 1, 3, 10, 30, and 100 µM. To evaluate the cytotoxic effect of guanylhydrazones, the MTT assay was also performed with GBM02 cells at the same concentrations, where the positive control was Temozolamide (TMZ). The selectivity index was calculated by the formula cytotoxic concentration in 50% of blood mononuclear cells/cytotoxic concentration in 50% of GBM02 cells. The migration assay was performed using Scratch, where microphotographs were used to obtain the migration percentage. For the study on morphology changes, GBM02 cells were plated and adhered to coverslips, with TMZ as a positive control and DMSO 0.2% as a negative control. Regarding the cytotoxicity assay against monocytes and lymphocytes, none of the compounds used were tested for toxicity and all findings were selective for tumor cells. As a result of the in vitro cytotoxic activity against GBM02, comparisons to the prototype were similar, except for LQM 242 (Table 1). Regarding the maximum inhibitory effect on GBM02 cells, the compounds in the series presented a cytotoxic effect greater than 70%, except for LQM 242 and LQM 244 in 48 hours of treatment. In the Scratch assay, we can observe that the compositions influenced the expansion of GBM02 migration, with LQM 14 standing out, which decreased migration by 88.09%, and LQM 240, which decreased it by 86.54%. Regarding morphology, the derivatives LQM 14 and LQM 240 (Figure 1) morphologically affected the neoplastic cells. Given the two, it can be observed that this series of results of compounds declared the capacity to be antitumor agents and to become future therapeutic options in the treatment of glioblastoma.

Table 1: Effect of guanylihydrazonic derivatives on GBM02 with 95% confidence index

Code	IC_{50} (µM)	CC_{50} (µM)	Selectivity Index (SI)
TMZ	>100	>100	>1
LQM 14	1,94	>100	>48,54
LQM 239	5,07	>100	>19,72
LQM 240	3,54	>100	>28,24
LQM 241	6,30	>100	>15,87
LQM 242	>100	>100	>1,0
LQM 243	4,15	>100	>24,09
LQM 244	22,74	>100	>4,39
LQM 245	8,85	>100	>11,29

Figure 1: GB02 morphology before (A and C) and after treatment with LQM 14 (B) and LQM 240 (D)