BIO043

Assessment of cytotoxicity and genotoxicity of the compound Monastrol in human hepatoma cell C3A.

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Introduction: Genetic toxicology assesses the effects of chemical and physical agents on DNA and on the genetic processes of cells. Pharmacological evaluations of new drugs include tests for mutagenicity and genotoxicity as parameters to determine health risks to humans. The majority of current antineoplastic drugs do not exhibit selectivity and, therefore, affect both healthy and tumor cells. Absence of selectivity and mechanism of resistance to apoptosis of tumor cells are factors that may hinder the success of chemotherapy, maximizing its side effects. Therefore, it is large to search for new molecules that act selectively against tumor cells in order to minimize effects. The motor kinesin related to mitosis stood out in this quest, and the protein EG5 have been studied for their potential for cancer therapy because of its importance for cell division and its overexpression in tumor cells compared with non-tumor cells. Monastrol is a synthetic diidropirimidinona, low molecular weight, cell-permeable with a inhibitory activity specific of protein EG5 and some studies have shown that this molecule interfere in the formation of the mitotic spindle and progression of the cell cycle, leading to inhibition of cell proliferation tumor. **Objective:** Therefore, the aims of this study was evaluate the genotoxic potential of synthetic compounds Monastrol in human liver carcinoma line, C3A, by Cytotoxicity Assay (MTT) and the Comet assay. **Methods:** For the cytotoxicity assay (MTT) The cells were plated in 96 well plates, which were tested 7 concentrations of the compound Monastrol (1, 10, 100, 200, 300, 400 and 500 μM) in two stages, 24 and 48 hours . After this test, three concentrations (1,10 and 100 μM) were choose for Comet assay and the cells were exposed for 3 hours. In Comet assay were analyzed 50 cells per slide. The damage and cytotoxic-inducing agent was Doxorubicin (1 μM). The data obtained by MTT assay and Comet assay were analyzed by Analysis of Variance (ANOVA) followed by Dunnett's test, using the program GraphPad Instat. **Results:** The data obtained shown that Monastrol was cytotoxic as compared to control ($p < 0.001$) in the concentrations of 200-500 μM in all treatment periods. After exposure for 48 hours, the concentration of 100 μM of Monastrol was cytotoxic ($p < 0.001$). In comet assay only 100 μM showed genotoxicity. **Conclusion:** Considering the results obtained, the cytotoxicity observed at concentrations up to 100μM for 48 hours and genotoxicity observed after exposure cells C3A to 100 μM of Monastrol suggests that the observed cytotoxicity has occurred in response to induction of the damage genetic material caused by this molecule. However, more studies are needed to understand the mechanism of action of this diidropirimidinona against tumor cells.

Keywords: Monastrol, C3A, Cell Cycle, Genotoxicity, Cytotoxicity.

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