THE PYRROLIZIDINE ALKALOID MONOCROTALINE INDUCES DNA DAMAGE BUT NOT PEROXIDATION IN GL-15 GLIOMA CELLS.

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It has been demonstrated that the pyrrolizidine alkaloid monocrotaline (MCT) is metabolised by hepatic cytochrome P450, and may generate metabolites capable of interact with macromolecules and initiate chronic or acute intoxication, which can leads intoxicated animal to develop neurological sings. In this study the ability of the MCT induces oxidative and genotoxic damages in GL-15 glioma cells was investigated. Confluent cell cultures, grown in DMEM supplemented medium, were treated for 72h with 1-500µM MCT. Cells treated with 0.5% DMSO were used as negative control, and cells treated with 0.3% hydrogen peroxide and directly exposed to UV light were used as positive controls. Peroxidation was investigated by measuring thiobarbituric acid reactive substances (TBARS). Cell DNA damage was evidenced by the Comet test. The presence hydrogen peroxide significantly increased peroxidation, raising the TBARS production from control levels of 0.07± 0.03 to 0.63±0.09nmol/mg protein. However, MCT did not alter the TBARS production. The results showed that 1µM MCT failed to induce a significant increase on cell DNA damage. However, exposure of cells to 10-500µM MCT caused significant increases in cell damage index, which reached 42-64%. The data obtained provide support that the alkaloid MCT acts directly on glial cells inducing DNA damage but not peroxidation of macromolecules. Supported by CNPq and CAPES.