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Use of Short Term Genotoxicological Tests to Study Cytotoxic, Genotoxic and Cell Death Mechanism of Metronidazole

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SUMMARY. Metronidazole (MTZ) is a wonderful drug, which is used clinically to treat a wide range of bacterial and protozoal infections. This study aimed to achieve a precise characterization of the cytotoxic and genotoxic activities of MTZ in cultured human lymphocytes at therapeutic concentrations and to evaluate the possible cell death mechanism associated with it. A significant decrease in Mitotic Index ($P < 0.001$) as well as an increase in Sister Chromatid Exchange ($P < 0.001$) and Chromosomal Aberrations ($P < 0.001$) frequencies with no modifications in Replication Index was observed. DNA extracts of MTZ treated cells resulted in nucleosomal DNA ladder pattern after 48 h of cell treatment and this pattern correlated with a decrease in cellular viability ($P < 0.001$), morphological evidence of apoptosis and increase in the percentage of nuclei with hypodiploid DNA content ($P < 0.001$). We concluded that MTZ is genotoxic, cytotoxic and is able to modulate cell death through apoptotic mechanisms in the experimental design employed.

KEY WORDS: Cell death, Cytotoxicity, Genetic toxicology, Genotoxicity, Metronidazole, Short term tests.

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