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GSH depletion, mitochondrial membrane breakdown, caspase-3/7 activation and DNA fragmentation in U87MG glioblastoma cells: new insight into the mechanism of cytotoxicity induced by fluoroquinolones

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Abstract

Fluoroquinolones are a known synthetic group of antibiotics that have been the subject of many research interests. This class of antibiotics was shown to be cytotoxic towards various cancer cell lines, thus representing a potentially important source of new anticancer agents. The present study was designed to examine the effect of ciprofloxacin and moxifloxacin on cell viability, redox balance and apoptosis in U87MG glioblastoma cells. Herein, we found that both fluoroquinolones decrease the viability and exert an anti-proliferative effect on U87MG cells. The EC₅₀ values were found to be as 0.75 µmol/ml, 0.57 µmol/ml, 0.53 µmol/ml for ciprofloxacin and 24, 48, 72 h incubation time, respectively, and 0.48 µmol/ml, 0.22 µmol/ml, 0.15 µmol/ml for moxifloxacin and 24, 48, 72 h incubation time, respectively. Ciprofloxacin and moxifloxacin have also induced the intracellular GSH depletion and apoptosis as shown by externalization of phosphatidylserine, caspase-3/7 activation, S and sub-G₁ cell cycle arrest, nuclear morphological changes induction and DNA fragmentation. The mechanism of apoptosis was related to the loss of mitochondrial membrane potential suggesting activation of the intrinsic mitochondrial pathway. This is the first study that may provide the basis for understanding potential cellular and molecular mechanism underlying ciprofloxacin and moxifloxacin cytotoxic and pro-apoptotic effect towards U87MG glioblastoma cells, suggesting that these fluoroquinolone derivatives may have value for the development as anti-glioma agents.

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