Antitumor effects of miconazole on human colon carcinoma xenografts in nude mice through induction of apoptosis and G0/G1 cell cycle arrest.

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Abstract

Miconazole (MIC), a promising oral antifungal agent, has been used worldwide in the treatment of superficial mycosis. In this study, we demonstrated that MIC dose dependently arrested various human cancer cells at the G0/G1 phase of the cell cycle. The protein levels of p53, p21/Cip1, and p27/Kip1 were significantly elevated by MIC treatment in COLO 205 cells. Electrophoretic mobility gel shift assays showed that the nuclear extracts of the MIC-treated COLO 205 cells exerted a significant binding between wild-type p53 and its consensus-binding site present in the p21/Cip1 promoter. These results suggested that the p53-associated signaling pathway is involved in the regulation of MIC-induced cancer cell growth arrest. By immunoblot analysis, we demonstrated that cyclin D3 and cyclin-dependent kinase-4 (CDK4) protein levels were inhibited by MIC treatment in the cancer cells. Significant therapeutic effect was further demonstrated in vivo by treating nude mice bearing COLO 205 tumor xenografts with MIC (50 mg/kg ip). The protein expression of p53 was significantly increased in MIC-treated tumor tissues by immunohistochemical staining and Western blotting analysis. DNA fragmentation and TUNEL assay were performed and demonstrated that apoptosis occurred in tumor tissues treated with MIC. Our study provides the novel mechanisms of antitumor effects of MIC and such results may have significant applications for cancer chemotherapy.