

題名:Induction of apoptosis and cell-cycle arrest in human colon cancer cells by meclizine

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摘要:Meclizine (MEC), a histamine H1 antagonist, is used for the treatment of motion sickness and vertigo. In this study, we demonstrate that MEC dose-dependently induced apoptosis in human colon cancer cell lines (COLO 205 and HT 29 cells). Results of a DNA ladder assay revealed that DNA ladders appeared with MEC treatment in COLO 205 cells at dosage of >50  $\mu$ M. In addition, the total cell number decreased dose-dependently after treatment with MEC in COLO 205 and HT 29 cells. Using flow cytometry, the percentage of COLO 205 cells arrested at G0/G1 phase increased dose-dependently. Analysis of changes in cell-cycle arrest-associated proteins with Western blotting showed that p53 and p21 were upregulated after treatment with MEC. The kinase activities of cyclin-dependent kinase 2 (CDK2) and CDK4 were suppressed in MEC-treated cells. As for apoptosis, MEC may induce upregulation of p53 and downregulation of Bcl-2, thus causing the release of cytochrome C from mitochondria and the translocation of apoptosis-inducing factor (AIF) to the nucleus. This resulted in the activation of caspase 3, 8, and 9. Our results provide the molecular basis of MEC-induced apoptosis and cell-cycle arrest in human colon cancer cells.