Effect of dihydroartemisinin on proliferation of human lung adenocarcinoma cell line A549
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【Abstract】 Background and objective Recent researches discovered that artemisinin and its derivatives had anti-tumor activity. Dihydroartemisinin is one of the derivatives with higher activity. This study is to explore the effect of dihydroartemisinin on the proliferation of human lung adenocarcinoma cell line A549, so as to provide experimental base for treatment of lung cancer. Methods Inhibition of proliferation in vitro was measured by MTT assay. The cell growth curve was drawn according to cell counts. The population doubling time was counted in logarithmic growth phase. DNA contents were measured by flow cytometry. Cell cycles were observed at the same time after the treatment. And the nude mice bearing A549 cancer cells were applied to detect the effect of dihydroartemisinin in vivo. Results Dihydroartemisinin inhibited A549 cell proliferation in a concentration-dependent manner. After 96 hours of treatment, the IC50 for dihydroartemisinin inhibition of cell number was 0.23 μmol/l. The population doubling time for human lung adenocarcinoma in the control group was 21.3 h and that in the dihydroartemisinin group was 38.5 h. An highly significant difference was observed between the two groups (P<0.01). Cells in G0 plus G1 were increased after the dihydroartemisinin treatment. The tumor inhibiting rate of dihydroartemisinin was 54.3% in vivo. Conclusion Dihydroartemisinin has marked anticancer activity on human lung adenocarcinoma cell line A549 both in vitro and in vivo. The inhibition in vitro is related to blockade of G0 and G1 phases.

【Key words】 Dihydroartemisinin Lung neoplasms Nude mice

This work was supported by Foundation of Xi’an Science And Technology Bureau (to QI Haowen) (SF-2002223).
1. **材料与方法**

1.1. CO₂发生器（中）Napoc-6100），450 ml CO₂（中）Bio-Rad）。

1.2. RPMI-1640（中）Gibco），（中）（中）MTT）、DMSO）Sigma）。

1.3. A549（中）（中）10%（中）100 μ/ml RPMI-1640（中）37°C、5% CO₂（中）< 0.1%）。

1.4. BALB/C(nu/nu) SPF）。4～6，20～24 g，25°C ± 2°C，(45%～50%)，4°C，10 mmol/l DMSO，37°C、5% CO₂（中）96 h。

1.5. RPMI-1640（中）DMSO（中）< 0.1%）。

1.6. 100 nmol/l A549（中）IC₅₀（中）2×10³）。12 h）（中）500 μl MTT）3200 nmol/l，1000 nmol/l，5 μl）。DMEM，37°C、5% CO₂（中）96 h。

1.6.1. A549（中）MTT）（中）2×10³）。12 h）（中）3.2.10、3200.1 000 nmol/l，5 μl）。DMEM，37°C、5% CO₂（中）96 h。

1.6.2. A549（中）IC₅₀（中）100 nmol/l，490 nm）。50 μl DMSO，4 h）。150 μl）。DMEM（中）10 min）。0.49 mm）。100 μl）。DMEM（中）0.49 mm。50 μl MTT）4 h，OD）（中）OD）×100%。

1.7. NOSA（中）1 ml）。
**Results**

Dihydroartemisinin has a significant inhibitory effect on the proliferation of human lung adenocarcinoma cells, and this effect is dose-dependent. The IC\textsubscript{50} value is less than 1\%.

**Discussion**

In the current era of chemotherapy, screening for antitumor drugs from natural products is a research hotspot. Dihydroartemisinin is a peroxide-bridged sesquiterpenoid lactone with a broad range of applications. With the deepening of its antitumor activity and related mechanism research, it is highly likely to become a new clinical antitumor drug.

This study showed that dihydroartemisinin has a significant inhibitory effect on the proliferation of human lung adenocarcinoma cells in vitro. Further studies are needed to explore its mechanism of action and the impact on the body's physiological functions.

Dihydroartemisinin has been administered orally to patients, and the blood concentration peak is much higher than the half-maximal inhibitory concentration in vitro. Cell death occurs in two ways: necrosis and apoptosis. Apoptosis is an active suicide activity driven by gene regulation. Excessive cell proliferation and blocked apoptosis are important biological characteristics of malignant tumors. Dihydroartemisinin can induce tumor cell apoptosis to play an antitumor role. From the cell cycle analysis results, it can be seen that the proportion of \( G_0 + G_1 \) cells increases, indicating that dihydroartemisinin can inhibit tumor cell mitosis.

In this study, we used BALB/c nude mice to establish a xenograft model of human lung cancer. After inoculation, all the mice survived, and the tumor formation rate was 100\%. The tumor induction period was about 10\, days. Histological examination confirmed it as adenocarcinoma, indicating that the xenograft model was successful. Further drug treatment was conducted. After oral administration of 2 mg/kg per day, the body weight of the mice was significantly reduced. After 96 h, the body weight was reduced to 71\% of the initial weight. The IC\textsubscript{50} value was 0.23 \( \mu \text{mol/l} \), and the maximum inhibitory effect was achieved. Compared with the control group, the average tumor weight of the treatment group was significantly reduced. The tumor inhibition rate was 54.3\%.
双氢青蒿素在实验周期内无明显毒性反应。逐步深化进一步深入研究！宿主的裸鼠的生物学特性有关。细胞在裸鼠体内的生长有显著性。试验结果表明现象。双氢青蒿素在治疗肺癌方面将具有良好的位或静脉接种有关。与体外实验结果一致。另外尚与肿瘤细胞本身和作为。