

鬼臼酰肼哌啶胺氮氧自由基和鬼臼乙叉甙对体外白血病 L7712 细胞核酸和蛋白质代谢的影响

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Podophyllic acid piperidyl hydrazone nitroxide radical and etoposide on nucleic acids and protein metabolism of leukemia L7712 cells *in vitro*

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ABSTRACT Podophyllic acid piperidyl hydrazone nitroxide radical (GP-1) and etoposide (VP-16), derivatives of podophyllotoxin, inhibited DNA, RNA, protein and ATP synthesis of leukemia L7712 cells at a concentration of 5 $\mu\text{g/ml}$. Inhibitory extents were dependent on the exposure time from 3 to 24 h. The inhibitory rates of both drugs were about 15-66%. ID_{50} of GP-1 and VP-16 on the synthesis of L7712 cells at 24 h were 0.16 and 0.38 $\mu\text{g/ml}$, respectively. The dose-response curve of GP-1 was a parabolic one, while that of VP-16 was a straight line. The inhibition of GP-1 or VP-16 on DNA synthesis existed also after cells washing. It is suggested that the antitumor effects of GP-1 and VP-16 seem to be related to the damage of DNA template.

KEY WORDS podophyllotoxin; free radicals; leukemia L 7712; cultured cells; adenosine triphosphate; [³H]thymidine; [³H]uridine; [³H]leucine; podophyllic acid piperidyl hydrazone nitroxide radical; etoposide

摘要 鬼臼酰肼哌啶胺氮氧自由基(GP-1)和鬼臼乙叉甙(VP-16) 5 $\mu\text{g/ml}$, 在体外能显著抑制小鼠白血病 L7712 细胞 DNA, RNA, 蛋白质和 ATP 的合成, 其抑制作用与时间正相关, 对 DNA 合成 24 h 的 ID_{50} 分别为 0.16 和 0.38 $\mu\text{g/ml}$. GP-1 的量-效关系呈曲线相关, VP-16 为直线相关。

关键词 鬼臼毒素; 自由基; 白血病 L7712; 培养的细胞; 腺苷三磷酸, [³H]胸苷, [³H]尿苷, [³H]亮氨酸, 鬼臼酰肼哌啶胺氮氧自由基, 鬼臼乙叉甙

鬼臼酰肼哌啶胺氮氧自由基 (podophyllic acid piperidyl hydrazone nitroxide radical, GP-1) 为鬼臼毒素 (podophyllotoxin) 的衍生物⁽¹⁾, 其抗肿瘤活性较鬼臼毒素强⁽²⁾, 体外实验 GP-1 和鬼臼乙叉甙 (4'-demethylpodophyllotoxin-9-(4, G-O-ethylidene-D-glucopyranoside, VP-16) 均可抑制癌细胞增殖。GP-1 增加细胞有丝分裂指数 (MI) 而 VP-16 则降低之^(3,4)。本文研究 GP-1 和 VP-16 对 615 小鼠白血病 L7712 细胞 DNA, RNA, 蛋白质以及 ATP 合成的影响。

MATERIALS

癌细胞 无菌取接种于 615 近交系小鼠 d 5 的白血病 L 7712⁽⁵⁾ 细胞 (上海医药工业研

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