

论著

维生素E琥珀酸酯体外防护顺铂肝细胞毒性并增强其抗肿瘤细胞增殖活性

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摘要 目的 研究维生素E琥珀酸酯(VES)对顺铂(CP)肝细胞毒性及联合用药增强抗肿瘤活性的可能。方法 用二步灌流法分离人和大鼠肝细胞, 接种于胶原铺被的96孔板, 细胞贴壁后, 分别加入一系列浓度的CP, VES及CP+VES, 于48 h用噻唑蓝(MTT)比色法检测细胞存活率, 并计算半数抑制浓度(IC_{50}) ; 同样方法用于检测CP, VES及CP+VES对人前列腺癌细胞系DU-145和人结肠癌细胞系CCL229的抗增殖作用。结果 CP, VES, CP+VES 1 mg \cdot L $^{-1}$, CP+VES 5 mg \cdot L $^{-1}$, CP+VES 10 mg \cdot L $^{-1}$ 对人肝细胞的 IC_{50} 分别为2.35, >100, 2.26, 4.25, 6.93 mg \cdot L $^{-1}$; CP, VES, CP+VES 5 mg \cdot L $^{-1}$, CP+VES 10 mg \cdot L $^{-1}$, CP+VES 25 mg \cdot L $^{-1}$ 对大鼠肝细胞的 IC_{50} 分别为4.70, >100, 10.94, 17.57, 23.24 mg \cdot L $^{-1}$; CP, VES, CP+VES 5 mg \cdot L $^{-1}$, CP+VES 10 mg \cdot L $^{-1}$, CP+VES 25 mg \cdot L $^{-1}$ 对DU-145和CCL229的 IC_{50} 分别为6.36, 55.36, 5.04, 4.85, 0.58和9.58, 39.47, 7.29, 4.22, 2.43 mg \cdot L $^{-1}$ 。结论 VES能明显减低CP所致人和大鼠肝细胞毒性, 增强CP对DU-145和CCL229细胞的抗增殖作用。

关键词 肝细胞 肿瘤细胞, 培养的 顺铂

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Vitamin E succinate ester prevents from cytotoxicity of cisplatin in hepatocytes and enhances its antiproliferative activities

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Abstract

AIM To investigate the effects of vitamin E succinate ester (VES) on cytotoxicity of cisplatin (CP) and to explore the possibility of enhancing antitumor activity by the combination of VES and CP. **METHODS** Hepatocytes isolated from rats and humans by two-step perfusions were used to evaluate cytotoxicity of CP and antiproliferative activity of CP in human prostate cancer cell line DU-145 and human colon cancer cell line CCL229; MTT assays were performed to evaluate cell viabilities. **RESULTS** Concentration of CP which inhibited 50% cell growth(IC_{50}) was 2.35 and 4.70 mg \cdot L $^{-1}$ in primary cultures of human and rat hepatocytes, respectively. VES increased IC_{50} of CP to 6.93 mg \cdot L $^{-1}$ and more than 100 mg \cdot L $^{-1}$, respectively; IC_{50} of CP in DU-145 and CCL229 were 6.36 mg \cdot L $^{-1}$ and 9.58 mg \cdot L $^{-1}$, respectively. VES decreased IC_{50} to 0.58 mg \cdot L $^{-1}$ and 2.43 mg \cdot L $^{-1}$, respectively.

CONCLUSION VES can decrease CP-induced cytotoxicity in human and rat hepatocytes, and enhance antiproliferative activity of cisplatin in DU-145 and CCL229.

Key words hepatocytes tumor cell cultured cisplatin vitamin E succinate ester

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