

论著

氧化吲哚类化合物Z24的体内抑瘤活性及其血管生成抑制作用

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摘要 目的 从抗血管生成活性的角度, 寻找新的抗肿瘤药物, 研究Z24的体内抑瘤活性及其对血管内皮细胞的选择性抑制作用。方法 MTT法检测不同浓度的Z24作用72 h时对人肝癌细胞系BEL-7402及正常人胚肺二倍体细胞2BS的生长抑制作用, 并从浓度-抑制率曲线求出IC₅₀; 台盼蓝拒染计数法检测不同浓度的Z24作用72 h时对人脐静脉内皮细胞(HUVEC)的生长抑制作用, 从浓度-抑制率曲线求出IC₅₀; 小鼠S180, H22和裸小鼠皮下移植性人肝癌BEL-7402模型研究Z24的体内抑瘤作用。鸡胚尿囊膜(CAM)血管生成模型检测Z24的血管生成抑制活性。结果 MTT法测得Z24对BEL-7402生长抑制作用的IC₅₀为106 μmol·L⁻¹, 对2BS生长抑制作用的IC₅₀为116 μmol·L⁻¹。台盼蓝拒染计数法测得Z24对HUVEC生长抑制作用的IC₅₀为6.44 μmol·L⁻¹。Z24可明显抑制鸡CAM新生血管的形成Z24 100 mg·kg⁻¹可使S180, H22和裸小鼠人肝癌BEL-7402模型的肿瘤重量较对照组分别下降52.5%(n=10, P<0.01), 41.5%(n=10, P<0.01)和53.4%(n=6, P<0.01)。Z24可显著抑制CAM的血管生成。结论 Z24对多种肿瘤动物模型均具有显著的体内抑瘤活性, 对血管内皮细胞有选择性抑制作用, 并明显抑制CAM新生血管的生成。

关键词 吲哚-2-酮类化合物, SU5416 血管生成抑制剂, Z24 药物筛选试验, 抗肿瘤 肉瘤180 肝细胞瘤 细胞系, BEL-7402

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Antitumor activity of an indolin-2-ketone compound Z24 *in vivo* and its anti-angiogenesis activity

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Abstract

AIM With the purpose of finding new antitumor drugs with anti-angiogenesis activity, the antitumor activity of Z24 *in vivo* and its anti-angiogenesis activity were investigated. **METHODS** MTT assay was used to determine the growth inhibitions of human hepatocellular carcinoma cell line BEL-7402 and pulmonary cells of fetus 2BS by Z24. Trypan-blue exclusion was used to measure the growth inhibition of human umbilical vein vascular endothelial cells (HUVEC) by Z24. Chorioallantoic membrane(CAM) assay was used to determine the anti-angiogenesis activity of Z24. Transplantable mouse sarcoma 180(S180), hepatoma 22 (H22) and human hepatocellular carcinoma cell line BEL-7402 models were used to evaluate the antitumor activity of Z24 *in vivo*. **RESULTS** The IC₅₀ values of Z24 for BEL-7402 and 2BS by MTT assay were found to be 106 μmol·L⁻¹ and 116 μmol·L⁻¹, respectively. The IC₅₀ value of Z24 for HUVEC by trypan-blue exclusion assay was 6.44 μmol·L⁻¹. Z24 at 100 mg·kg⁻¹ inhibited the growth of subcutaneous S180, H22, and BEL-7402 tumors by 52.5%(n=10, P<0.01), 41.5%(n=10, P<0.01), and 53.4%(n=6, P<0.01), respectively. **CONCLUSION** These results suggest that Z24 present high antitumor activity *in vivo*, can selectively inhibit vascular endothelial cells, and have anti-angiogenesis activity on CAM.

Key words indoles-2-ketone compounds SU5416 angiogenesis inhibitors Z24 drug screening assays antitumor sarcoma 180 hepatoma cell line BEL-7402

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