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论文

手性钌配合物的合成、抗肿瘤活性及其与血清蛋白的相互作用

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摘要:

合成了手性钌配合物Δ, Λ-$[Ru(bpy)_2(pyip)]^{2+}$, 通过元素分析、核磁共振、质谱和CD光谱对配合物进行了表征. 采用MTT法评价了3种异构体对多种肿瘤细胞株的体外抗肿瘤活性以及对正常细胞的毒性. 结果表明, Δ-$[Ru(bpy)_2(pyip)]^{2+}$的抗肿瘤活性明显优于其异构体, 对A375, SW480, MCF-7和A549的半数抑制浓度低于顺铂. 通过荧光光谱法研究了在生理pH条件下, 手性钌配合物与牛血清白蛋白(BSA)之间的结合作用以及荧光猝灭机制. 依据Scatchard方程测定了结合常数和结合位点数, 根据热力学方程讨论了两者间的主要作用力类型. 结果表明, 钌配合物对牛血清白蛋白的荧光猝灭机制为静态猝灭. Δ-1, 1和Λ-1与牛血清白蛋白的结合常数分别为1.16×10^5, 5.12×10^4和3.64×10^4, 结合位点数均为1, 主要作用力类型是静电作用. 钌配合物在体内能够被血清蛋白存储转运且结合时对蛋白构象无影响.

关键词: 手性钌配合物; 抗肿瘤活性; 牛血清白蛋白

Synthesis and in vitro Anticancer Activities of Chiral Ruthenium Complexes and Interaction of the Complex with Bovine Serum Albumin

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Abstract:

Chiral ruthenium(Ⅱ) complexes Δ-$[Ru(bpy)_2(pyip)]^{2+}$ and Λ-$[Ru(bpy)_2(pyip)]^{2+}$ were synthesized and characterized in detail by elemental analysis, ^{1}H NMR, electrospray ionization mass spectrometry(ESI-MS) and circular dichroism(CD). The *in vitro* anticancer activities of the ruthenium(Ⅱ) complexes were screened by MTT assay. The results show that Δ-$[Ru(bpy)_2(pyip)]^{2+}$ exhibited higher cytotoxic effects against human cancer cells. The quenching mechanism of the fluorescence of bovine serum albumin (BSA) by chiral ruthenium(Ⅱ) complexes was investigated by fluorescence spectroscopy under simulative physiological conditions. The binding constant *K* and the number of binding sites were determined according to Scatchard equation and the main binding force was discussed *via* thermodynamic equations. The experimental results show that the quenching mechanism of chiral ruthenium(Ⅱ) complexes to bovine serum albumin was static quenching. The binding constants *K* were 1.16×10^5, 5.12×10^4, 3.64×10^4 L·mol^{-1} with one binding site, respectively. The binding force is electrostatic interaction. Chiral ruthenium complexes have nearly no effect on the serum protein conformation.

Keywords: Chiral ruthenium complex; Anticancer activity; Bovine serum albumin

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