Gold(I) and platinum(II) with isocyanide ligand complexes: Synthesis and biological activity

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Technology description

In our first project, new Pt(II) complexes were synthesized by the reaction of the precursor complexes cis,cis-[Me2Pt(μ-SMe2)2PtMe2], and cis-[(p-tolyl)2Pt(SMe2)2], with four and two equivalents of different types of isocyanide ligands (CNR; R = a; t-butyl, b; benzyl, and c; cyclohexyl isocyanide), respectively. All complexes were characterized by FTIR and NMR spectroscopies, and the structure of one of the Pt complexes was confirmed by single-crystal X-ray determination. The evaluation of the cytotoxicity of Pt complexes against three human cancer cell lines, namely A549 (non-small cell lung cancer cell line), SKOV3 (human ovarian cancer cell line), and MCF-7 (human breast cancer cell line), revealed promising antitumor activities for two of the Pt complexes in comparison with that of the standard cisplatin. Moreover, one of the Pt complexes effectively rendered apoptosis-inducing activities to the MCF-7 cancer cell line. The electrophoresis mobility shift assays on plasmids as well as molecular docking studies on DNA structures effectively revealed the specific binding site, binding mode, and the best orientation of the complexes to DNA.

In our second project, the reaction of [(Me2S)AuCl] with an equimolar amount of benzyl isocyanide (PhCH2NC) ligand led to the formation of complex [(PhCH2NC)AuCl] (1). The solid-state structure of 1 was determined using the X-ray diffraction method. Through a salt metathesis reaction, the chloride ligand in 1 was replaced by pyrimidine-2-thiolate (SpyN−) to afford the complex [(PhCH2NC) Au(η1-S-Spy)] (2), which was characterized spectroscopically. The cytotoxic activities of 1 and 2 were evaluated against three human cancer cell lines: ovarian carcinoma (SKOV3), lung carcinoma (A549) and breast carcinoma (MCF-7). Complex 2 showed higher cytotoxicity than cisplatin against SKOV3 and MCF-7 cancer cell lines. It showed a strong anti-proliferative activity with IC50 of 7.80, 6.26 and 6.14 μM, compared with that measured for cisplatin which was 7.62, 12.36 and 11.47 μM, against A549, SKOV3 and MCF-7 cell lines, respectively. The induction of cellular apoptosis by 2 was also studied on MCF-7 cell line. Our results indicated that 2 could induce apoptosis in cancerous cells in a dose-dependent manner.

Technology:

Cisplatin and its analogues, specifically, carboplatin and oxaliplatin, are well-known chemotherapeutic drugs, while nedaplatin, lobaplatin, miriplatin, and heptaplatin are subsequently developed as potential chemotherapeutic agents. These compounds are important clinical chemotherapeutic drugs and they vital role in cancer treatment, but the usage of these drugs have severe side effects on normal cell lines

and produce serious problems like hematological toxicity and neurotoxicity, and also some solid tumors have gained resistance to them. The disadvantages and limitations of the current drugs have highly encouraged organometallic and biomedical research to concentrate on the discovery of new platinum compounds. In this regard, some platinum complexes have been synthesized and tested on various cancer lines. Most of these compounds were excluded in primary clinical steps of treatment due to their toxicity. Therefore, finding of novel platinum drugs that are less toxic and more selective than current commercial available drugs against of the resistance tumors are extremely demanded. As a result there is a continuous research to discover new platinum-based drugs with lower toxicity and also to get around the body resistance towards the current commercial drugs.

Application area

The complexes have the potential to be commercialized as anticancer drugs. The gold complexes can also be considered as antimicrobial agents as well.

Advantages

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Because of the development of body resistance towards platinum anticancer drugs, on the other hand, novel gold-based anti-tumor complexes with pharmacological characteristics other than Pt-based drugs are important targets in modern drug design and medicinal chemistry. In recent years, Au-based complexes have received increasing consideration because of their potent inhibition of cancer cell growth which is mainly caused by non-cisplatin-like mechanisms of action. In this regards, again at the same time we are working on the development of gold-based drugs as they show less toxicity and have a different

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