Synthesis and Biological Activity Evaluations of Novel Heterobimetallic Platinum(II)–Gold(I) Complexes as Bio-imaging Agents.

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Abstract

Introduction: Platinum-based drugs have become a mainstay of cancer therapy, approximately half of all patients undergoing chemotherapeutic treatment receive a platinum drug. Despite the pervasiveness of platinum drugs in cancer treatment regimens, a number of attendant disadvantages such as resistance to some cancer types and side effects exist. Gold complexes are also emerging as a new class of metal complexes with outstanding cytotoxic properties and are presently being evaluated as potential antitumor agents.

Methods and Results: Here, some novel heterobimetallic platinum(II)–gold(I) complexes were synthesized and their cytotoxic activities against different human cancer cell lines such as A549 (human lung cancer),
SKOV3 (human ovarian cancer) and MDA-MB-231 (human breast cancer) were evaluated. Electrophoresis mobility shift assay and molecular modeling investigations have been performed to determine the specific binding mode or the binding orientation of these compounds to DNA. Molecular docking studies of them on DNA were performed by means of AutoDock 4.2. Fluorescence emission properties of them were assessed using fluorescent microscopy imaging.
In comparison to cis-platin, these compounds displayed significantly higher *in vitro* cytotoxicity on the studied cell lines. They enter SKOV3 cells rapidly, retaining their phosphorescence and localise simultaneously in cytoplasm, especially in perinuclear regions. So they are suitable candidates for time resolved emission imaging microscopy (TREM). Electrophoresis mobility shift assay showed a little shift and little interaction with plasmid DNA, though this shift is not as much as cis-platin. They may exert their cytotoxic effect through a different mechanism.

Conclusions: According to the results, careful drug design would result in producing potential antitumor agents with high efficacy. These Pt(II)-Au(I) complexes can be used in biological labelling and cellular imaging studies, due to desirable absorption and emission of them in solution under ambient conditions. Hence, they had a potential value for drug development as anticancer agents.

Key words: Bio-imaging; Cytotoxic activity, Platinum(II)–Gold(I) complexes, DNA binding, Molecular docking.

Grants: Ahvaz Jondishapur University of Medical Sciences.