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CISPLATIN INDUCES REACTIVE OXYGEN SPECIES, CHANGED GLUTATHIONE LEVELS, AND ACTIVATES APOPTOSIS IN HUMAN ACUTE LEUKEMIA CELLS

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Abstract: Cisplatin (cis-diammine-dichloro-platinum II) is an organometallic- platinum compound centering two adjacent chlorine and amine atoms that was initially discovered to prevent the growth of *E. coli* and was further recognized for its anti-neoplastic and anti-tumor effects upon cancerous cells. Cisplatin is administered intravenously in humans and by oral route in mice; and is used as first-line chemotherapy treatment for patients diagnosed with various types of malignancies, such as leukemia, lymphomas, breast, testicular, ovarian, head and neck, cervical, and sarcomas. In the present study, we used human acute myeloid leukemia (KG1a) cells as a model to investigate the cisplatin-induced reactive oxygen species (ROS), changed glutathione levels, and early apoptosis. We hypothesized that cisplatin may induce ROS, effect glutathione levels, and initiate the apoptotic pathway. To test our hypothesis, we measured reactive oxygen species (ROS), reduced glutathione(GSH) levels, and early apoptosis after 24 hours incubation of KG1a cells with different concentrations (5, 10, 20, 40, and 80 μM) of cisplatin at 37^0C using spectrophotometric and fluorescence techniques. After incubation, we investigated an increase in ROS production at concentrations of 10 μM and 20 μM. The Glutathione Detection Assay revealed cisplatin lowered glutathione levels. Results from the Apoptosis Annexin V Assay also indicated that early events of apoptosis, or cell death was concentration-dependent manner. Our findings showed that cisplatin induces ROS production by reducing reduced GSH levels and activated early apoptosis in KG1a cells. It may help to develop a new anti-leukemic drug designing or enhanced toxicity of existing drugs to kill leukemia cells more efficiently.

Key words: Cisplatin, reactive oxygen species, glutathione, apoptosis, KG1a cells

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