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PHARMACOLOGY OF CISPLATIN AS AN ANTI-CANCER AGENT

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Cis-platin, also known as cis-diamminedichloroplatinum (II), is an anticancer or DNA-destroying drug with a square planar cis configuration. It is one of the first platinum-based drugs that the FDA approved as an anticancer drug. It has long been acknowledged as one of the most frequently prescribed cytotoxic anticancer medications with extensive efficacy. The platinum-based drugs work by preventing tumor cells' DNA from replicating and transcription, which in turn prevents cell proliferation and apoptosis. It is used to treat lymphomas, germ cell tumors, sarcomas, carcinomas, and other types of cancer. In the treatment of tumors, cisplatin is typically given intravenously as a brief infusion with normal saline. It is known that cis-platin based non-specific chemotherapy can cause toxic side effects such as nausea, nephrotoxicity (a dose-limiting side effect), hepatotoxicity, cardiotoxicity, and neurotoxicity (in some patients, impaired hearing and perception).

The rule of activity includes cytotoxic impacts on growth cells by arrangement of DNA adducts or DNA cross connections of mono, inter or intra-strand, that captures the cell in the cell cycle period of S, G1 or G2-M stage prompting cell apoptosis. The death of carcinogenic tumor cells is attributed to the impairment in DNA replication caused by this condition. Apoptosis is influenced by a number of factors, including phosphatidylinositol 3 kinase, p53 tumor suppressor gene facilitated by protein, and Bcl2 proteins. Cisplatin's therapeutic efficacy could be enhanced with the help of these insights. Caspase activation is the mechanism by which apoptosis is carried out at the molecular level. The intracellular cysteine proteases known as caspases cleave substrates at aspartic acid residues. During the subsequent activation of caspases, certain compounds, known as inhibitors of apoptosis protein (IPAs), prevent cell death. Because they shield tumor cells from both intrinsic and extrinsic apoptotic pathways, IPAs are a major obstacle in the cisplatin-based treatment of cancer.

Evidence indicates that numerous patients relapsed and developed resistance to chemotherapy despite cisplatin's therapeutic efficacy. This kind of conflict occurs when growth cells fail to undergo apoptosis at the specified clinical convergence of cisplatin drugs. Cisplatin-resistant cancer cells' increased cross-resistance also contributes to the difficulties and complexity of chemotherapy. As a general rule, opposition can be a consequence of openness to persistent medications or natural cell changes. Some of the underlying mechanisms include decreased drug accumulation in cells, increased DNA repair, or cytosolic inactivation of cisplatin (an impairment in efficacy caused by substances like glutathione or thiol-containing molecules).

Cisplatin-based chemotherapy is known to cause common side effects like nausea and vomiting as well as toxic side effects that affect a variety of vital organs. Numerous harmful impacts like arrhythmias, congestive cardiovascular breakdown, ECG changes or even myocarditis were found in a couple of cases. According to one study, patients who did not receive antiemetic medication prior to taking cisplatin developed an average of 11 episodes of vomiting after receiving a 120mg/m2 dose of the drug. Because cisplatin has a tendency to accumulate in the proximal part of the kidneys, nephrotoxicity is another significant side effect. Increased kidney reabsorption and inhibition of carnitine production, a substance involved in the transport of fatty acids from the cytosol to mitochondria, constitute another mechanism. Cisplatin is transported into cells via two primary membrane transporters, OCT2 and Ctrl1. Once in the kidney, cisplatin undergoes biotransformation to cysteinyl glycine conjugates and other higher thiols that is believed to cause toxicity.

In conclusion, we realized the significance of cisplatin therapy as the foundation for treating various cancers. Even though most cancer cells respond well to platinum chemotherapy, cisplatin resistance frequently causes relapses in many patients.