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**BCH 410 ASSIGNMENT**

1. **ROLE OF CISPLATIN AS ANTICANCER AGENT**

Cisplatin (cis-Diamminedichloroplatinum II or CDDP) is one of the most important chemotherapeutic agents widely used in treatment of many types of solid cancers including testicular cancer, ovarian cancer, cervical cancer, breast cancer, bladder cancer etc. This compound was first synthesized in 1845 by Peyrone, but its antitumor activity was discovered by accident by Rosenberg, the physics teacher at the University of Michigan in the late 1960s. Cisplatin is a white or yellow crystalline powder, slightly soluble in water and soluble in dimethylpyrimidine and N, N-dimethylformide. It is a neutral inorganic molecule with molecular weight of 301.1 g/mol, density of 3.74 and melting point at 270°C. it is composed of platinum ion bound to two ammine groups and two chloride ions that are arranged in a square. The ammine groups represent carrier ligands, while chloride ions are leaving groups. In cisplatin the chlorides are next to each other. The presence of leaving groups is essential for biological activity of cisplatin. Inside the cell, cisplatin loses two chloride ions and they are replaced by loosely bound water molecules, allowing the platinum to attack the DNA molecule in nucleus. Cisplatin interferes with DNA replication, which kills the fastest proliferating cells, which in theory are cancerous. Cisplatin was indeed demonstrated to possess antitumor activity in a mouse model and was first used in the clinical trial almost 30 years ago. Since its approval by the Food and Drug administration in 1978, cisplatin continues to be one of the most effective anticancer drugs used in the treatment of solid tumors. It is also used as an adjuvant therapy following surgery or radiation. In addition to cisplatin, its analogs, such as carboplatin and oxaliplatin, are also currently being used in the clinic. The antitumor activity of cisplatin is believed to be due to its interaction with chromosomal DNA. Only a small fraction of cisplatin, however, actually interacts with DNA and the inhibition of DNA replication cannot solely account for its biological activity. In addition, the efficacy of chemotherapeutic drugs depends not only on their ability to induce DNA damage but also on the cell's ability to detect and respond to DNA damage. Following DNA damage, cells may either repair the damage and start progressing through the cell cycle or if they cannot repair the damage, cells proceed to die. Cisplatin, like many other chemotherapeutic drugs, can induce apoptosis. Thus, the signaling pathways that regulate apoptosis have significant impact on deciding cellular responsiveness to cisplatin. There are many excellent reviews on cisplatin and its analogues.

1. **ROLE OF VANADIUM AS ANTI-DIABETIC AGENT**

Vanadium is a trace mineral that is present in many foods and may be essential in small amounts in the body. It may be involved in normal bone growth. Vanadium has atomic number of 23, atomic weight of 50.94, it is a first-row transition metal that shows a wide range of oxidation states in monomeric, oligomeric, and polymeric species in solution. It exists in oxidation states of −I, 0, +II, +III, +IV, and +V; the latter two are stable solution structures at physiological pH i.e. vanadyl (+IV) and vanadate (+V). Vanadate has insulin-like effects on the metabolism of glucose both invivoand in vitroin various tissues. Vanadium salts such as Na3VO4, NaVO3, VOSO4 etc. mimic several of the metabolic and growth-promoting effects of insulin. Vanadium salts like sodium orthovanadate, sodium metavanadate, and vandyl sulfate have insulin like action and they lower blood glucose levels in various animal models and act as potential hypoglycemic agents. Vanadium activates the glycogen synthase and tyrosine kinase activity of the insulin receptor in adipocytes. It increases the concentration of fructose 2,6-biphosphate and activates glycolysis in hepatocytes. Vanadium also stimulates glycogen synthesis in muscle. The oral administration of vanadate by streptozotocin induced diabetic (STZ-D) rats causes normalization of hypoglycemia

and tissue responsiveness to insulin. Vanadium salts at doses ranging from 0.1 to 0.7 mM/kg/day normalized blood glucose and lipid levels, improved insulin sensitivity, and impaired antioxidant status and fluid intake. Absorption, distribution, metabolism, and excretion (ADME) of vanadium compounds are reported as a chronic treatment alternative for diabetics. However, treatment of diabetic animals with inorganic vanadium salts has also been associated with some toxic side-effects such as gastrointestinal discomfort and decreased body weight gain. In addition, vanadium salts have been reported to exert toxic effects on the liver and kidney. More recently, it was shown that organic vanadium compounds were much safer than inorganic vanadium salts and did not cause any gastrointestinal discomfort, hepatic or renal toxicity.

1. **ROLE OF SELENIUM AS ANTI-CANCER AGENT**

Selenium (Se) is regarded as an essential element playing a key role in human health and its deficiency results in many pathological processes and diseases, including cancer. Selenium is an essential element in the structure of selenocysteine which is necessary for the proper functioning of several enzymes and that in general sufficient supplementation of Se as a part of diet leads to inhibition of tumorigenesis and to decreased risk of cancer. Methylated forms of Selenium such as Se-methylselenocysteine, methaneselenenic, or methaneseleninic acid, are usually able to contribute to the cellular protective mechanisms that may result in tumor prevention. Typical examples of such compounds are selenomethionine and selenocysteine derived from methionine and cysteine respectively. These two amino acids are part of selenoproteins such as glutathione peroxidases, thioredoxin reductases and iodothyronine deiodinases some of which participate in processes of apoptosis, cell growth and modulate cell signaling systems and transcription factors. The chemopreventive anticancer effect of Selenium and Selenium-containing compounds is based on their ability to act as antioxidants as well as modulate the immune system. Selenium in selenoproteins helps to protect organisms from the consequences of oxidative damage as glycoprotein glutathione peroxidase reduces biological peroxides to alcohols and also reduces free hydrogen peroxide to water. Selenium in physiological cellular concentrations exhibits its anti-oxidative properties that is an integral of all ROS-detoxifying selenoenzymes, especially selenocysteine containing enzymes. High concentrations of Selenium may be used for cancer chemoprevention as the antioxidative effects of selenoenzymes and pro-oxidative effects of some other Selenium containing substances in tumor cells may result in a reduction of carcinogenic processes and also in an introduction of some anti-carcinogenic processes. Selenium as a chemo preventive agent has an ability to increase the therapeutic effects or decrease toxic side effects of some clinically used antineoplastic agents which allow new treatment options of applying combinations of anti-cancer agents with Selenium. selenomethionine exhibits protective effects in anticancer therapies because of its antioxidative properties and also because of its ability to modulate processes of DNA repair. In general, selenomethionine causes a decrease in DNA damage of cells exposed to cytotoxic agents. In a case of colon cancer, mechanisms of action of Selenium that may take place in colon cancer chemoprevention are the inhibition of cyclooxygenase and cytosine methyltransferases, interaction with carcinogens and the activation of P53 which leads to dependent growth inhibition through apoptosis.