

Study on Cisplatin' s Role in the Combat with Cancer

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ABSTRACT. *As a not only famous but also effective cancer drug, cisplatin plays an extremely vital role in the combat with cancer, one of the most fierce illnesses in the world. This thesis lays most of its emphasis on cisplatin's physical and chemical properties, as well as its discovery process and curative effects.*

KEYWORDS: *cancer, cisplatin*

Birth

In the cancer wards of National Institutes of Health Clinical Center in 1976 that like a clean version of hell, with artificial gaiety exaggerated by orange walls in corridors, yellow and white striped rooms, and cartoon smiley buttons clipped to the nurse uniforms, as well as the lingering and atmosphere of death, cisplatin, a drug disguised as poison, first appeared. To patients, cisplatin is the epitome of a new variety of radical chemotherapy drugs in the 1970s. Treatments that added this molecule possessed a remarkable and lasting effect unprecedented in the history of cancer treatment alone with persistent nausea and vomiting, so strong that was also rare in the history of medical science.

Cisplatin is short for cis-platinum, modified from an inherent drug. Its molecular structure has been described as early as the 1980s: with platinum atom as the center, four "arms" extend around. This orange crystalline powder is made up of two amino groups and two Chlorine atoms----there is no doubt that it has an extreme beautiful as well as strictly symmetric molecular structures. However, chemists had never discovered its application value. It was left in the laboratory in obscurity, and no one bothered to test its biological effects.

Excavation

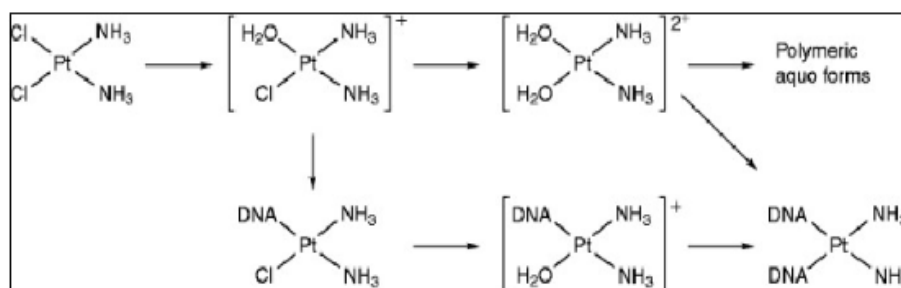
The year when this chemical compound, which can be called an artwork born in the God-like hands of the nature, started to unfold its illustrious treasure to the world was 1965. A biophysicist called Barnett Rosenberg of the Michigan State University initiated his study of whether electric current can stimulate cell division.

In order to succeed in the experiment, Rosenberg created a bacteria culture bottle especially designed for this test, a special one that could utilize two platinum electrodes to power on. He turned on the simply constructed power supply, whereas he did not make a full psychological preparation to usher in a totally unexpected result-the cell division stopped completely. At first Rosenberg thought that electric current was the active factor that inhibited cell division, but it soon became clear that the current was just an outsider.

The whole experiment had a quite dramatic plot. In the legend of science, people often describe the exciting second of "the moment of great scientific discovery" with the rapid heartbeat and extraordinary brilliance, when all of a sudden, the observation results were clear and transparent, converging into a new form. Just like the fragments of a phantoscope abruptly been shaped up. What Rosenberg was going through was a bit similar to this literary description. He found that the platinum electrodes interacted with the salts from bacteria solution. From this quick process, a brand novel growth inhibiting molecule was born and it further spread to the whole solution. Just like other cells, the division of bacteria also requires DNA replication. Cisplatin is able to use its chemical active molecular arms to offend DNA molecules[3]. It can be bonded to bases in DNA and form three types of cross-linking that irreversibly damages those big molecules that contain significant life information making the bacteria stop splitting themselves[4].

Application

Cisplatin's name first emerged in the therapeutic schedule in October 1st, 1974.



In other words, at this point of time, cisplatin impressed its name deeply in the world of cancer, as one of the most powerful weapons toward cancer, the enemy that humanity has always been fighting against since we were born from a single cell. A 22-year-old veterinary, John Cleland, diagnosed his Metastatic testicular carcinoma in 1973. At that time, the survival rate of Metastatic testicular carcinoma was less than 5 percent. Cleland was admitted to a cancer ward at Indiana University and began his treatment by a young oncologist Larry Einhorn. The treatment was a cocktail of three toxic drugs called "ABO," a painful and ineffective drug derived from research at the National Cancer Institute in the 1960s. He was discharged, hospitalized and tossed back and forth and his weight dropped rapidly from 72 kg to 48 kg. One day in 1974, his wife advised him to go out and sit in the warm, smiling

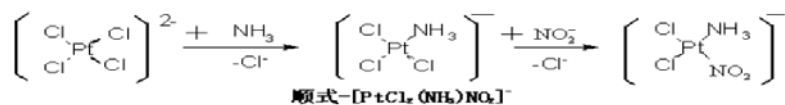
sunshine after an afternoon of chemotherapy. Then he realized that he was too weak to stand up. He was carried to bed like a baby, and this cognition made him cry helplessly. In the autumn of the same year, the ABO program ended. Einhorn suggested that they should make every possible effort and recommended a new drug called cisplatin. On one hand, there are uncertain new drug combinations; on the other, there is inevitable death. Cleland decided to take the risk: he was registered as "patient 0" for the BVP program that included bleomycin, vinblastine and cisplatin[5]. Ten days later, when he returned to the hospital for a routine scan, the tumor in the lung disappeared. Overjoyed and confused, he called his wife on the hospital phone: "I don't remember what I said, but I told her the good news."

Cleland's experience is typical. By 1975, Einhorn had treated another 20 patients with this regimen[1], and it became increasingly clear that some of those patients would never relapse. "It's unforgettable. I naively thought this was the recipe we had been looking for but couldn't."

Cisplatin is equally impressive in other ways. It seems crazy but on average, patients taking this drug vomit 12 times a day. In Margaret Edson's play *Wit*, she vividly depicts women's struggle against ovarian cancer: the British professor who is undergoing chemotherapy holds on to the vomiting basin and retches painfully. Then her unforgettable voice over sounded, "you might think my vocabulary has degenerated." The culprit behind the scenes is cisplatin.

Although these side effects are obnoxious, the cost to its miraculous effect is small. In the late 1970s, cisplatin was sold in large quantities as a chemotherapeutic product. This is a classic example of confronting cancer patients with the danger of death and then encouraging them to fight to live. Until now, this molecule, which is nearly 40 years old, still has an unshakable position in chemotherapeutic drugs. Compared with other complicated organic substances, the unsophisticated step of adding ammonia to K_2PtCl_4 to synthesize

Cisplatin makes it possible to be widely used[2].



"Extreme measures may cure a fatal disease, or it may not work at all," William Shakespeare wrote in his most celebrated drama *Hamlet*. Growth is a sign of cancer, but it is also a sign of life. Cisplatin will still turn back to a poison disguised as drug eventually. Humanity is determined to fight against cancer, and we are already on a path where there is no turning back. This tiny molecule is only an epitome of a four-thousand-year war in which there is no lack of victories and defeats, protracted campaigns, heroes and cowards, survivors and relapses. We must fight till the end, and must not rest until this battle is won.

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