GOLD NANOPARTICLES AS CARRIERS OF CISPLATIN: A NEW APPROACH FOR CANCER TREATMENT

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At the nanoscale, materials exhibit unique optical, electronic and magnetic properties not seen at the bulk scale, which makes nanostructures attractive for a wide range of applications. The combination of these unique properties with the appropriate size scale has motivated the introduction of nanostructures into biology.[1] Cells and their constituent organelles lie on the sub-micron to micron size scale. Further, proteins and macromolecules found throughout the cell are on the nanometer scale. Thus nanoparticles ranging from a few to a hundred nanometers in size become ideal as labels and probes for incorporation into biological systems.[1] Furthermore, surface chemistry facilitates the functionalization and integration of nanoparticles. This opens the door to a wide variety of applications in molecular biology and biomedicine, such as drug[2] and gene delivery,[3] tissue engineering,[4] protein and DNA sensing[5] and detection-based diagnostics,[6] and biological/biomedical imaging.[7] Furthermore, noble metals, especially gold (Au), have a great potential for cancer diagnosis and therapy mainly due to their surface plasmon resonance (SPR) enhanced light scattering and absorption. One of the main challenges in cancer research is to minimize the side effects of chemotherapeutic drugs while maintaining their potency against cancer cells. In particular, cisplatin is widely used for the treatment of a variety of tumors, including lung, head and neck, testis, and ovarian cancers.[8-10] Chemotherapy is often associated with toxicity and/or severe side effects and damaging of healthy tissues at the vicinity of the tumors. Cisplatin is believed to kill cancer cells by binding to DNA and interfering with its repair mechanism,[11] eventually leading to cell death. Cisplatin has encountered the same fate as many other drugs used in cancer chemotherapy, namely drug resistance. When cells become resistant to cisplatin, the doses must be increased; a large dose escalation can lead to severe multiorgan toxicities (such as failures of the kidneys and bone marrow), intractable vomiting, and deafness. Therefore, it has been proposed the development of AuNP-cisplatin conjugates to overcome drug resistance while increasing the amount of drug inside malignant cells. The AuNP will act as transporters of the drug and delivery systems once they are at the tumor site. The generation of these new drugs involved the synthesis and characterization of water soluble-cisplatin derivatives as well as the preparation of the final conjugated molecules (AuNP-cisplatin conjugates) (Scheme 1). These conjugates are administrated to tumor cellular lines (HeLa, HEK and A459) to test their ability to decrease the side effects caused by the original drug.

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Figures:

Scheme 1: Schematic representation of the synthetic strategy to generate AuNP-Cisplatin conjugates