



Recent applications of nanotechnology in advanced drug delivery systems

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Abstract

Nanotechnology is attracting great attention worldwide in biomedicine. Targeted therapy based on drug nanocarrier systems enhances the treatment of tumors and enables the development of targeted drug delivery systems. In recent years, theranostics are emerging as the next generation of multifunctional nanomedicine to improve the therapeutic outcome of cancer therapy. Polymeric nanoparticles with targeting moieties containing magnetic nanoparticles as theranostic agents have considerable potential for the treatment of cancer. The use of Directed Enzyme Prodrug Therapy (DEPT) has been investigated as a means to improve the tumor selectivity of therapeutics. Magnetic DEPT involves coupling the bioactive prodrug-activating enzyme to magnetic nanoparticles that are then selectively delivered to the tumor by applying an external magnetic field. Gene therapy is an attractive method for meeting the needs for curing brain disorders, such as Alzheimer's disease and Parkinson's disease. On the other hand, due to the fact that Hepatocellular Carcinoma (HCC) is resistant to standard chemotherapeutic agents, gene therapy appears to be a more effective cure for HCC patients. Ultrasound-mediated drug delivery is a novel technique for enhancing the penetration of drugs into diseased tissue beds noninvasively. This technique is broadly appealing, given the potential of ultrasound to control drug delivery spatially and temporally in a noninvasive manner.

Cancer is considered the second most frequent cause of death worldwide after cardiovascular disease. Although great improvements have been made in cancer therapy, it is still a major health concern and, therefore, various investigations have been done to develop new therapeutic approaches.

Cancer involves uncontrolled growth of cells and it can develop in any tissue. The basic process of different types of cancer is similar; it begins when a cell has a faster rate of cell division than normal cells. The initiation of cancer is highly linked to oxidative stress that results in DNA damage,

instability of genome and cell proliferation. Various researchers have reported the mechanism by which oxidative stress can lead to chronic inflammation, which leads to many diseases including cancer.

Compared to normal cells, cancer cells have a concentration of endogenous reactive oxidative stress (ROS). Low concentrations of ROS compounds are required for signal transduction, but a cancer cell has an accelerated metabolism, thus they need high ROS concentrations to maintain their high proliferation rate. They cause damage in mitochondrial DNA, which leads to mutation in the oxidative phosphorylation resulting in increase in production of ROS. It aids in the proliferation of cancer cells, which leads to an increase in tumor growth. That is why cancer cells require high ROS concentrations to maintain their high proliferation rate.

ROS damage in cells depends on their intracellular concentration and on the equilibrium between the ROS and the endogenous antioxidant species. Oxidative stress is generated as a result of the loss of the pro-oxidant/anti-oxidant equilibrium. This oxidative stress alters and damages many intracellular molecules such as proteins, lipids, DNA and RNA.

The generation of oxidative stress is caused by the imbalance between reactive oxidative stress production and the deficiency of the cell antioxidant defense system. This imbalance leads to damage of important cells as it affects the whole organism. Many forms of chemotherapy and radiation therapy act through oxidative stress pathways. Various researchers have reported the mechanism by which oxidative stress can lead to chronic inflammation, which leads to many diseases including cancer.

Reactive oxygen species (ROS) are products of metabolic reactions in the mitochondria of eukaryotic cells. Low concentrations of ROS compounds are required for signal

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Various studies reported that cancer patients showed low antioxidant level and increased oxidative stress, even before start of the treatment. Sharma et al. has evaluated patients with tongue carcinoma, results showed that pretreatment levels of plasma lipid peroxide and conjugated dines were significantly elevated in patients with carcinoma, as compared with controls.

Antioxidants are effective in scavenging free radicals. The first definition of antioxidant was proposed by Halliwell et al. as "any substance that, present in low concentrations compared to oxidizable substrates (carbohydrates, lipids, proteins or nucleic acids), significantly delays or inhibits the oxidation of the mentioned substrates". Antioxidants attract a huge interest in cancer therapy, where they eliminate oxidizing free radicals, thus prevent cellular damage, which is helpful in chemotherapy. Different articles have investigated antioxidant supplements during chemotherapy in order to protect normal tissues without adversely influencing tumor therapy.

There are two kinds of antioxidants doses used in cancer therapy: a preventive low dose, which provides protection of normal cells and tumor cells and a therapeutic high dose, which inhibits the growth of cancer cells without affecting normal cells. Recent reviews proved that administration of antioxidants with chemotherapy has the following advantages: (a) they do not interfere with chemotherapy and (b) they improve the cytotoxic effect of chemotherapy while protecting the normal tissue thus increases the patient survival and therapeutic response.

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