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Pt/ TiO_2 CATALYSTS IN THERAPEUTIC APPLICATIONS

Biochemistry

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ABSTRACT

Nanotechnology involved in the design, synthesis, characterization, and application of materials and devices whose functional organization is at the nanoscale. Cancer is one of the leading causes of death worldwide; it is a condition in which the use of nanotechnology has been studied for diagnostic and therapeutic purposes. The conventional approach to treatment includes chemotherapy and radiotherapy, which is limited by its toxicity to neighboring normal cells, the resistance of cancer cells and the proliferation of tumors due to the presence of stem cells. In this study we determine the effect of platinum catalysts supported on nanoparticles (NPs) of titanium dioxide (TiO2) in tumor cells. Transmission electron microscopy and fluorescence microscopy studies confirm a synergistic effect between the inorganic oxide support of TiO2 and the platinum drug, which reduces the rate of tumor growth due to the apoptotic effect of the tumor cells without associated adverse events.

KEYWORDS

Nanostructures, Nanomedicine, Tumors, Catalysis

Introduction:

According to the International Organization for Standardization (ISO), Nanotechnology is the application of scientific knowledge to manipulate and control matter in the nanoscale in order to make use of size and structure-dependent properties and phenomena, as distinct from those associated with individual atoms or molecules or with bulk materials. The nanoscale-size range is defined between 1 and 100 nm (Ref to ISO ISO/TS 80004-1:2015). The main attractive of Nano science is the potential to control and manipulate matter in nanometers; size that is compared to the molecular structures that comprise the biological systems of the human body. (2,3)

Nanomaterials have been studied and developed to explore applications in medicine, particularly in cancer research. (4) Cancer is one of the leading causes of death worldwide, less than half of patients diagnosed have a 5-year survival period. Conventional treatment, chemotherapy and radiotherapy are limited by their toxicity to normal cells, the resistance of cancer cells to the development of drugs and the proliferation of the tumor due to the presence of tumor stem cells. (5)

The use of nanotechnology in the cancer field allows more effective administration of the drug, with higher and localized doses, in addition to reducing the side effects caused by chemotherapy and radiotherapy. In particular, the development of nanoscale devices (dendrimers, micelles covered with silicon, nanoparticle ceramics, among others) as carriers / release of these drugs is one of the most significant advances in recent years for cancer therapy. (6,7,8)

The sub-nanometer size of these devices promotes cell uptake by endocytosis. A notable advantage of ceramic nanoparticles is the hydrophilic nature of the surface, which favors stealth effect through the reticuloendothelial system, preventing its degradation in the bloodstream (9) In addition, the proper design of the nanoparticle synthesis allows to modify the specific surface area, the pore size distribution and the acid-base properties, to tailor made de NP to a specific application. These characteristics drastically change the way we diagnose, treat and prevent cancer. (8,10)

Hypothesis:

Embryonic stem cells represent a study route applicable to various diseases, but due to the ability to self-renew and differentiate into various types of specialized cells, the use of stem cells as an alternative treatment represents adjacent risks; they can pose problems derived from the generation of tumors. Tumors caused by embryonic stem cells have a rapid development and consist of derivatives of the three germ layers: ectoderm, endoderm and mesoderm.

The application of inorganic oxide nanoparticles allows the selective administration of drugs to tumor cells. The hydrophilic behavior of the surface prevents reticuloendothelial recognition and the intrinsic stability of this material avoiding degradation in the bloodstream It is possible that with the use of these particles in brain tumors provide clues for the development of nanoparticles of inorganic carrier drugs with high selectivity for the treatment of cancer and minimal side effects.

Based on these premises, the aim of the study is assess the effect of Pt catalysts supported on titanium dioxide (TiO2) nanoparticles in the development of tumors caused by embryonic stem cells in the central nervous system of mice.

Evaluation of the hypothesis

Pt(NH3)4Cl2 complex has been deposited in the TiO2 carrier by the sol-gel method, thus allowing the immobilization of the Pt(NH3)4Cl2 complex without any alteration of the crystalline structure of the inorganic oxide or texture. The platinum complex interacts with the TiO2 surface through the OH groups, reducing the number of acid sites, which infers the formation of specific interactions between the platinum complex and the TiO2 surface. The combination of the TiO2 nanometer material and the platinum complex reduces the rate of tumor growth, a side effect of cytotoxicity of platinum drugs mediated by the induction of apoptosis and the cell cycle inhibition given by the interaction with DNA. The drug Cisplatin generates cross-links of DNA, which results in the detection of mitosis, cellular DNA digestion and apoptosis. (11)

The nanoparticle of TiO2 at the morphological level of the cells generates changes that include rounding, sporadic distribution and loss of adhesion. The fluorescence microscopy study has allowed to relate the cytotoxic effect of the TiO2 nanoparticle, however this effect is dose dependent. Muthuraman Pandurangan et al demonstrated that the percentages of the apoptotic cell were 35, 54 and 59% with 2.4 and 8 mg / ml of TiO2 nanoparticles respectively. Cell apoptosis can be defined in a classical way by certain morphological characteristics and

biochemical characteristics that differentiate it from other forms of cell death. DNA fragmentation is a pathognomonic sign of apoptosis, endonuclease cleaves DNA into multiple fragments of chromatin in nucleosomal units, which appear as a DNA ladder, which is evidenced in cells treated with TiO2 nanoparticles. (12)

Empirical data:

We prepared a Pt(AcAc)2/TiO2 catalyst using the sol-gel method. The catalyst was prepared to maintain a loading of the active species (Pt) of 2% by weight. Characterization studies using X-ray photoelectron spectroscopy (XPS) confirm the presence of a single band with a binding energy of 72.8 eV, attributed to oxidized Pt.

The transmission electron microscopy studies (Figure 1) show that the titanium oxide support is completely amorphous. In addition, the inability to observe Pt nanoparticles in transmission electron microscopy wizards corroborate the presence of oxidized Pt, according to the XPS results.

Once the characterization was complete, the Pt(AcAc)2/TiO2 catalyst has been studied in non-symptomatic mdf / ocd mice (mice with a neurodegenerative disease similar to human sporadic amyotrophic lateral sclerosis). In particular, there have been three different sets of experiments. In a group of experiments, embryonic stem cells were transplanted into the bone marrow of mice (control individuals). In a second group, embryonic stem cells were transplanted together with catalyst nanoparticles and, finally, a last group of experiments was carried out, in which stem cells were transplanted, the tumor was expected to develop for 7 days and then the nanoparticles were introduced. All mice belonging to the three groups mentioned above were sacrificed 10 days after transplantation to process their tissues.

Visual observations indicate the absence of side effects and, in particular, the absence of paralysis in the lower extremities (due to tumors) in mice injected with Pt /TiO2 nanoparticles.

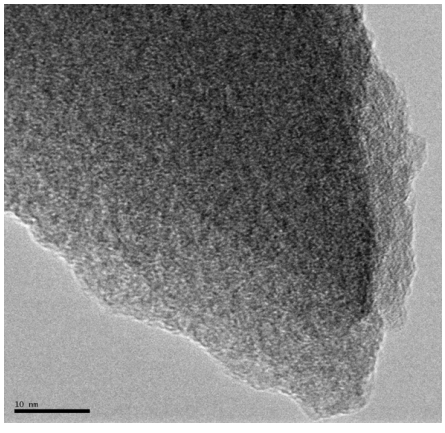

Figure 1. Transmission electron microscopy image, corresponding to the catalyst Pt (AcAc) 2 / TiO_2.

Consequences of the hypothesis and discussion

The implementation of nanotechnology in medicine and particularly in the diagnosis and treatment of cancer, allows the development of new treatment alternatives, where they have proven to be more effective than conventional therapy with radiotherapy and chemotherapy, this is given by the selectivity to tumor cells and decrease in associated adverse events.

The use of catalytic nanoparticles such as TiO2 carriers of platinum drugs, have a potential use as a chemotherapy agent with reduced toxicity, since the effect of inorganic oxygen carriers potentiate selectivity, contribute to the induction of apoptosis of cells tumors requiring less therapeutic doses.

Conflicts of interest

The authors declare that there is no conflict of interest.

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