

## **Poly(Amidoamine) Dendrimer-Cisplatin Nanocomplex Mixed with Multifunctional Ovalbumin Coated Iron Oxide Nanoparticles for Immuno-Chemotherapeutics with M1 Polarization of Macrophages**

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**Abstract :** Enhancement of drug efficacy is essential in cancer treatment. The immune stimulator ovalbumin (Ova)-coated citric acid (AC)-stabilized iron oxide nanoparticles (AC-IO-Ova NPs) and enhanced permeability and retention (EPR) based tumor targeted 4.5 (4.5G) poly(amidoamine) dendrimer-cisplatin nanocomplex (4.5GDP-Cis-pt NC) were used for enhanced anticancer efficiency. The formations of 4.5GDP-Cis-pt NC, AC-IO, and AC-IO-Ova NPs have been examined by FTIR, X-ray diffraction, Raman, and X-ray photoelectron spectroscopy. The conjugation of cisplatin (Cis-pt) with 4.5GDP was confirmed using carbon NMR. The tumor-specific 4.5GDP-Cis-pt NC provided ~45% and 28% cumulative cisplatin release in 72 h at pH 6.5 and 7.4, respectively. A significant immune response with high TNF- $\alpha$  and IL-6 cytokine secretion was confirmed when the co-incubation of AC-IO-Ova with RAW 264.7 or HaCaT cells. AC-IO-Ova NP was biocompatible in different cell lines, even at a high concentration (200  $\mu\text{g mL}^{-1}$ ). In contrast, AC-IO-Ova NPs mixed with 4.5GDP-Cis-pt NC (Cis-pt at 15  $\mu\text{g mL}^{-1}$ ) significantly increased the cytotoxicity against the cancer cells, which is dose-dependent on the concentration of AC-IO-Ova NPs. The increased anticancer effects may be attributed to the generation of reactive oxygen species (ROS). Moreover, the efficiency of anticancer cells may be further assisted by induction of an innate immune response via M1 macrophage polarization due to the presence of AC-IO-Ova NPs. We provide a better synergistic chemoimmunotherapeutic strategy to enhance the efficiency of anticancer of cisplatin via chemotherapeutic agent 4.5GDP-Cis-pt NC and induction of proinflammatory cytokines to stimulate innate immunity through AC-IO-Ova NPs against tumors.

**Keywords :** cisplatin-release, iron oxide, ovalbumin, poly(amidoamine) dendrimer

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