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Development of Platinum-loaded, Selenium-doped Hydroxyapatite Nanoparticles for Potential Application in Bone Tumor Therapy

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Bone is a common site for metastases derived from non-osseous tumors with high morbidity. Bone metastases cause uncontrolled bone formation or resorption. Since systemic antitumor chemotherapy can lead to severe side-effects, a strategy to overcome these drawbacks consists in the delivery of cytostatic drugs from locally implanted bone substitute materials. Among bone substitute materials, hydroxyapatite (HA) is well known for its biocompatibility and capability to load a wide variety of therapeutic agents. In particular, we focused on the incorporation of SeO_3^{2-} ions into HA[1] nanocrystals due to their ability to kill cancer cells by generation of reactive oxygen species. Moreover, a combination therapy with two or more drugs could offer the opportunity to synergistically improve the curative effect and overcome shortcomings of traditional chemotherapy. Since Pt-compounds are well known antitumor drugs (*i.e.* cisplatin, carboplatin, and oxaliplatin), we have developed platinum-loaded, selenium-doped hydroxyapatite nanoparticles. A series of Se-doped HA nanoparticles with different Se concentration has been synthesized and characterized and then loaded with [Pt(dihydrogenpyrophosphate)(*cis*-1,4-DACH)] (DACH = diaminocyclohexane), an hydroxyapatite-binding antitumor platinum complex. The chemotherapeutic activity of the platinum-loaded, selenium-doped hydroxyapatite nanoparticles has been tested *in vitro* against human prostate or breast cancer cells co-cultured with human mesenchymal stem cells[2].

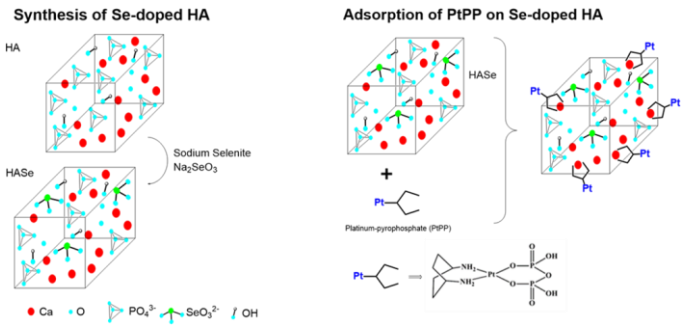

Figure 1. Schematic representation of Pt loaded HASe nanoparticles.

[1] A. Barbanente et al., *J. Inorg. Biochem.* 215 (2021) 111334.
[2] A. Barbanente et al., *J. Mater. Chem. B*. 8 (2020) 2792–2804.

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