CYTOTOXICITY OF HYDROXYAPATITE DOPED NANOPARTICLES ON OSTEOSARCOMA

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Introduction
Hydroxyapatite nanoparticles have recently been proposed as anticancer drug. Their cytotoxicity is associated to the sudden increase in calcium and phosphate ions inside cancerous cells following nanoparticle degradation. However, before nanoparticles (NPs) can enter the cell they first interact with the cell culture medium and the cell membrane and this could already alter cell behaviour. The present work seeks to disclose the contribution of each effect on cell cytotoxicity to have a better understanding of the mechanisms behind the use of NPs on cancerous cells.

Experimental
Hydroxyapatite doped nanoparticles were prepared by neutralisation of calcium hydroxide with phosphoric acid. Magnesium chloride was added in the reaction vessel to obtain magnesium doped nanoparticles. Cytotoxicity studies were performed assessing cell morphology and measuring the lactate dehydrogenase activity of cells in various scenarios: a) upon supplementing NPs on cells (direct contact), b) upon supplementing the NPs in inserts to avoid direct contact with cells but allowing any exchange of ions and molecules across the insert membrane (indirect assay), and c) by culturing cells on disks made compacting NPs to favour cell membrane interaction but avoiding internalisation.

Results and Discussion
The study demonstrated that cell viability was not affected when NPs were placed inside inserts proving that any exchange of ions between NPs and the medium was not toxic to cells. In addition, direct seeding of cells on top of disks made of compacted nanoparticles showed excellent cell adherence and spreading proving that they were not cytotoxic. However, when NPs we added in the cell culture media in direct contact with the cells, these died in less than 3 h due to NPs internalisation.

Conclusions
The results obtained in this work highlight the importance of NPs internalisation above other potential mechanisms of interaction and reinforces the need of improving internalisation in views of using these NPs for cancer treatment.

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