Biological characterization of nanocomposite hydrogels

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The effectiveness of systemically administered antineoplastic or antiangiogenic drugs is limited by difficulties in achieving therapeutic doses within tumors, concurrently to low side effects. At the present, one of the most innovative strategy for targeted drug delivery consists in coupling the drugs to nanomaterials such as nanoparticles (NPs). However, this technique present several problems including the toxicity of NPs *per se* and the possibility of drug deactivation once it is chemically bound to the NP.

To bypass these problems novel hybrid magnetic hydrogels containing magnetic $CoFe_2O_4$ or Fe_3O_4 NPs, as a crosslinker agents of carboxymethylcellulose, have been synthesized and loaded with drugs (Pasqui et al., 2011; Barbucci et al., 2012). The overall aim of this work was to investigate the biological properties of these hydrogels. In particular, we analysed the toxicity of the NPs hydrogels *per se*, in cultured human breast cancer (MDA-231) and human microvascular endothelial cells (HUVEC), and the release of cytotoxic drug, such as methylen blue (MB) and doxorubicin (Dox), by both types of hydrogels in *in vitro* studies. The release of MB and Dox from loaded NPs hydrogels was sustained in vitro over 7 days after an initial burst, indicating that NPs hydrogels acted as a drug depot. Consistently, drug-loaded NPs hydrogels exhibited marked in vitro anti-proliferative activity against both MDA-231 and HUVEC cells. By comparison, free Dox almost completely decreased cell viability in a time dependent manner. Conversely, incubation up to 7 days of unloaded-NPs hydrogels with cultured MDA-231 and HUVEC cells, did not induce significant cytotoxic activity.

In conclusion the findings show that: 1) NPs when included in hydrogels do not induce *per se* cytotoxicity; 2) NPs hydrogels act as a drug depot and are able to release cytotoxic drugs over time without affecting their efficacy.

References

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