Abstract

The development of nanodrugs applied to cancer therapy is a promising field in biomedicine which involves different scientific disciplines such as biology, materials science, chemistry, medicine and pharmacy. The aim of the clinical application of these materials is to overcome the wide range of limitations associated with conventional treatments, as limited therapeutic effectiveness and severe side effects.

This PhD study has been focused on the synthesis of silica based nanodrugs for the intracellular diffusion and controlled release of the antineoplastic agent camptothecin.

Firstly, several nanomaterials were synthesized applying the sol-gel method. Moreover, four different prodrugs were obtained in order to incorporate them on the previously synthesized materials trough a covalent bond. After a complete characterization of the nanodrugs, its robustness was tested on physiological media.

In order to study the release mechanism of the drug, experiments were carried out under different stimuli. Four kinetic models were chosen in order to study the release kinetics. It was found that diffusion mechanism in granular matrices was the main physicochemical parameter involved in the drug release.

Afterwards, the nanodrug antineoplastic activity was tested by cell viability assays, showing a similar toxicity to the free drug. In addition, flow cytometry assays were carried out in order to investigate which characteristics have an influence on cell internalization. Results showed that large hydrodynamic diameter and high hydrophobicity enhance cell internalization.

Finally, biodistribution, tolerability and therapeutic efficiency were tested *in vivo* in a human colorectal tumor cell xenograft in mice.

Despite an intensive nanodrug uptake by the reticuloendothelial system cells, the nanodrug accumulation in the tumor improved the treatment effectiveness when comparing to the free drug. Besides, side effects where minimized when using the nanodrug.

The results of this study lead the way to a new generation of drug based on hybrid organic-inorganic nanomaterials, creating new highly effective and selective cancer therapies.