Polyoxometalate-chitosan nanogels for breast cancer therapies

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Abstract

Tumour recurrence is one of the most serious limitations of current hormonal breast cancer treatment. Polyoxometalates (POMs) are anionic metal-oxo clusters that have recently shown to be capable of inhibiting signalling pathways in cancer stem cells *in vitro* [1], which is a key factor for resistance to estrogen mediated therapy. One of the main drawbacks of POMs as anticancer agents is their cytotoxicity and the difficulty to be incorporated into the cell. In order to improve both aspects it is necessary the development of nanocarriers which encapsulate them and ensure both the protection of the anticancer agent in healthy physiological environment, and the specific release inside tumour cells.
Chitosan nanogels constitute a good approach to stimuli-responsive nanodevices because of their unique properties: biocompatibility, biodegradability and pH-sensitive behaviour, as well as their structure of three-dimensional networks.
Chitosan is a biopolymer which behaves as a soluble cationic polyelectrolyte in acidic solutions due to the protonation of their glucosamine units. Consequently, chitosan networks swell at acidic pH, while remain collapsed at physiological pH.
Besides, it is well known that the pH of tumoral tissues is small but significantly lower than that of healthy ones[2]. Therefore, pH-sensitive gels have emerged as interesting drug nanocarriers [3]. This is the case of chitosan nanogels whose swelling at acidic pH would contribute to a high loading and specific POM release in tumoral sites, avoiding the damage in the surrounding healthy tissues.
Following this approach, Wells-Dawson type POMs $K_6[P_2Mo_{18}O_{62}]$ were successfully encapsulated into water dispersable chitosan-based nanogels. Nanoparticles were prepared by covalent crosslinking reaction of chitosan with poly(ethylene eglycol bis(carboxymethyl)ether), in reverse microemulsion medium. Loading efficiency of the POM was determined to be close to 90%. The release profile was also studied and a controlled release under different pH conditions was observed. Experimental results enhance the potential use of the prepared particles as nanobiomaterials for more effective therapies in the total eradication of breast tumours.

References

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Figures

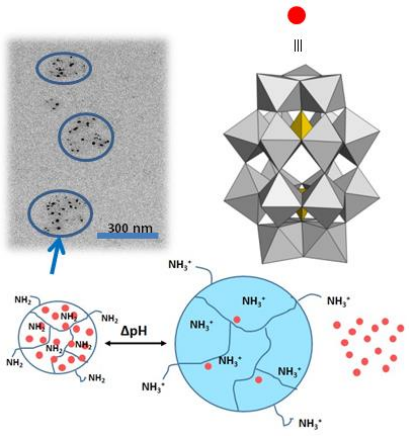

Figure 1: pH-sensitive POM release for chitosan nanogels.