Stimuli-Responsive Polypeptide Hydrogels for Targeted Drug Delivery Against Pancreatic Cancer

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Pancreatic cancer tumors are quite difficult to cure even nowadays. Injectable hydrogels constitute a very promising system, in order to achieve effective and selective delivery of chemotherapeutic drugs to cancer cells. The drug carrier should present multiple functions the most important being: a) implant the formulation into the body without surgical operation, b) prolong the drug release kinetics from the carrier, c) expand the type of drugs which can be delivered, d) minimize the patient's morbidity. [1] The only materials that can be organized at such a hierarchical level, besides natural proteins, are polypeptides especially due to their sensitive stimuli response. [2] Most of these systems take advantage of the higher temperature and lower pH of the malignant tissue. Thus, the polymer-drug mixture, when injected it is transformed from liquid to hydrogel within the tissue and releases the drug slowly in a controlled manner. Polypeptides are composed of repeating amino acids, connected by an amide bond and they adopt the 3D structures found in natural proteins, such as a-helices and β-sheets. In this work, a series of different polypeptide hydrogels containing poly-histidine, poly-lysine, poly-sarcosine and poly-L-glutamic acid have been synthesized. For this reason, the Ring Opening Polymerization of the corresponding N-Carboxyanhydrides of the amino acids was contacted. [3] Hydrophobic histidine provides pH and temperature responsiveness in the hydrogel, which in combination with the hydrophilic blocks of the poly-lysine and poly-sarcosine, results in an effective drug delivery system. Size exclusion chromatography, proton nuclear magnetic resonance and infrared spectroscopy were employed for the characterization of the synthesized polypeptides. Circular dichroism was carried out to study the correlation between the secondary structure, pH and temperature. All these techniques demonstrate the promising properties of these well-defined materials.

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