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# Development of a [99mTc]Tc-PVP nanogel for controlled release of 5-FU

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In most cancer treatments, chemotherapy is currently necessary. However, clinical anticancer drugs provoke serious side-effects. Nanogels (NGs) can efficiently improve cancer therapy increasing the antineoplastic concentration in tumor sites and without affecting normal tissues considerably. The aim of this work is developing a pH responsive polyvinylpyrrolidone(PVP)-based nanogel for controlled release of 5-fluorouracil (5-FU) that can be labelled with 99mTc. This formulation could be useful for in vivo imaging and assess the optimization of 5-FU dosages for each patient. The PVP nanoparticle was synthesized via gamma irradiation. Its potentiality as anticancer drug delivery system was demonstrated theoretically and experimentally using drug-nanoparticle docking, FTIR-ATR, UV-vis, XPS, TGA, TEM and DLS techniques. In vitro 5-FU release tests were performed simulating gastric, colon and intestinal conditions and drug release profile was fit employing empirical kinetic models. A direct radiolabelling approach was selected for obtaining the [99mTc]Tc-PVP nanoparticle formulation. The NGs have negative surface charge, spherical morphology and diameter of 45.1nm which is favorable for 5-FU entrapment. Computational simulations show a higher drug-polymer affinity at low pH in accordance with experimental loading values (EE =17.04% and DL=83.15%). The sustained release profile responds to the change of pH from 1.2 to 7.4 increasing release rate at acidic conditions. Protein-protein docking simulations and biocompatibility assays showed no interactions with seric proteins, no cytotoxic effects and no inflammatory immune response. According to gel permeation chromatography the radiolabelling efficiency of the employed methodology was 90%.

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