Development of smart carrier systems and their assessment for tumor targeted delivery of Capecitabine

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Abstract

Background: Colorectal cancer (CRC) is one of the most common cancers worldwide. Due to the general nature of chemotherapeutic agents systemic biodistribution and the ensuing side effects brought on by the drug targeting both normal and intended cell types make cytotoxic anticancer treatments a unique issues. In order to target the drug moiety directly to the damaged tissue and/or cells with the least amount of drug release at physiological sites, innovative drug delivery systems must be developed.

Objectives: In the present study, chitosan-g-poly (N-isopropylacrylamide-co-N-Vinylpyrrolidone) (CS-g-P(NIPAAm-co-NVP)) co-polymer sensitive to temperature and pH has been synthesized and evaluated its targeting ability to cancerous site by using anti-cancer drug Capecitabine.

Methods:CS-g-PNIPAAm-co-NVP co-polymers were synthesized using free radical copolymerization method with differing concentrations of chitosan and NVP and optimized its thermo and pH responsive properties to tumor microenvironment conditions by using 3^2 factorial design. Capecitabine was efficiently loaded into the optimised co-polymer and evaluated.

Results: The drug release was significantly increased *in vitro* when the tumour extracellular pH and temperature were used instead of physiological pH and temperature conditions. MTT assay also demonstrated enhanced drug release in the tumour microenvironment conditions. Fluorescence microscopic study showed that the cell uptake was significantly enhanced in tumor microenvironment. The nanoparticles are much more stable at 4-8±2°C, according to stability studies done on optimized formulation.

Conclusion: In conclusion, the discovered polymer in nanoparticles form appeared to have tremendous promise for the delivery of Capecitabine to specific tumours.

Keywords: Capecitabine, Chitosan, poly (N-isopropylacrylamide), N-vinylpyrrolidone, temperature responsive co-polymer, Lower critical solution temperature.