DRUG DELIVERY SYSTEMS FOR OVERCOMING MULTIDRUG RESISTANCE

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Abstract

Our main objective was to prepare the tumour-targeted polymer nanocarriers containing the inhibitors of multidrug resistance (MDR) along with the cytostatic agent. These systems may significantly improve the problematic treatment of the tumours with the MDR evolved due to the previous therapy using common cytostatic agents.

The prepared nanotherapeutics for overcoming MDR are polymer conjugates with the P-glycoprotein (P-gp) inhibitor ritonavir and the anticancer agent doxorubicin (DOX). The P-gp is a membrane-associated molecular pump transporting various substrates across the cellular membranes. The P-gp-driven cellular efflux of anticancer drugs (e.g. DOX) may lead to their reduced cytostatic activity. The over-expression of P-gp in cancer cells causes their MDR and consequently the ineffectiveness of the following cytostatic treatment. The use of the P-gp inhibitors is known as a possible way how to overcome MDR.

To overcome the MDR several polymer conjugates with DOX and ritonavir which differed in the spacer structure between ritonavir and the polymer carrier in order to prepare the most potent polymer-drug-inhibitor conjugate were synthesised and characterized. In vitro experiments are under way, but preliminary results are promising. The polymer nanomedicine bearing DOX as well as ritonavir is believed to be quite potent in the treatment of the tumours with the MDR.

Keywords: HPMA copolymers, cancer treatment, MDR, doxorubicin, controlled release

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