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Polymer nanotherapeutics to overcome multidrug resistance

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Multidrug Resistance (MDR) is one of the main causes of imperfect treatment of many types of haematological malignancies and solid tumours. The resistance of cancer cells to current chemotherapy is associated with the overexpression of at least two ATP-dependent efflux pumps (P-gp and MRP1) which participate in the preferential active transport of cytotoxic drugs out of the cells before the therapeutic effect. An inhibition of the overexpressed proteins described before should improve the retention of chemotherapeutics inside tumour cells, and thus a more effective cancer therapy can be achieved. It has been previously found that the high-molecular weight polymer carriers and their polymer-drug conjugates are subject of passive accumulation in solid tumours due to enhanced permeability and retention effect. Here, we present design, synthesis and evaluation of physico-chemical and biological characteristics of novel block copolymers serving simultaneously as drug delivery systems and MDR inhibitors. The amphiphilic character of presented copolymers changed their self-assembling into polymer micelles with an increased hydrodynamic radius in aqueous solutions. Cytostatic drug is bound to the copolymer through a pH-sensitive bond enabling a prolonged circulation in blood, the delivery of drug into solid tumour and controlled release of drug within tumour mass and cells at a decreased pH. The applicability of polymer nanotherapeutics as a drug carrier was confirmed by an *in vivo* biological evaluation. We observed significantly higher accumulation of micellar conjugates with drug in a solid tumour because of the EPR effect compared with the similar polymer-drug conjugate that do not form the micellar structure or with the parent free drug. MDR inhibition of the copolymers was verified by *in vitro* tests. In addition, we observed highly increased rate of the uptake of micellar nanotherapeutics within the cells.

Biography

Alena Braunová has completed her PhD in 2006 from Institute of Macromolecular Chemistry, Academy of Sciences of the Czech Republic (IMC). She is working as Senior Researcher at the Department of Biomedical Polymers of IMC. She has published 14 papers in reputed international journals, which were cited more than 98 times and she is an author or co-author of more than 40 international conference contributions and abstracts. Her research focus is based on preparation of micellar and water-soluble drug delivery systems for effective treatment of cancer and cancer diagnostics.

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