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Block copolymers of poly(*N*-2-hydroxypropyl methacrylamide) and poly(propylene glycol) - The way to inhibit P-glycoprotein?

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Tumour cell resistance tomultiple cytotoxic drugs(multi-drug resistance, MDR), especially to anthracycline antibiotics, is one of the main causes of imperfect efficacy of chemotherapy in current medicine. MDR is a protective response of tumour cells caused by long-term effect of drugs onto the cells. The cells could then decrease the drug intracellular concentration by various mechanisms - e.g. by drug effluxusing special transmembrane proteins, particularly P-glycoprotein (P-gp). P-gp is an ATP-dependent efflux pump of xenobiotic compounds with wide substrate specificity and it is a member of a family of ATP-binding cassette transporters. While in healthy cells P-gpeffluxesxenobiotics and toxins, in tumour cells, where P-gp is expressed in much higher amount, contributes P-gp due to this property frequently to MDR. Therefore, P-gp inhibition should cause a better drug penetration into the cells, and thus more effective cancer therapy.

Our work is focused on the synthesis of amphiphilic block polymer-drug conjugates, where one block is based on hydrophilic poly(*N*-2-hydroxypropyl methacrylamideand the other is hydrophobic derivative of poly(propylene glycol), which should be responsible for P-gp inhibition. These blocks form particles due to their different physico-chemical properties and thereby polymer-drug-conjugate molecularweight increase. This fact should be an advantage for passive targeting of these systems preferentially into solid tumours due to the Enhanced Permeability and Retention effect. The drug doxorubicin is boundedto the conjugate by pH-sensitive hydrazone bond, good degradable inside the cells (pH 5.0) but more stable in bloodstream (pH 7.4). Cell viability assay on MDR cancer cell lines are under way.

Biography

Alena Braunova has completed her PhD in 2006 from Institute of Macromolecular Chemistry, Academy of Sciences of the Czech Republic (IMC). She is a member of Department of Biomedicinal Polymers of IMC. She has published 12 papers in reputed international journals, which were cited more than 60 times and she is an 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 cancerdiagnostics.

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