

New Stimuli-Responsive Copolymers for Smart Drug Delivery Systems (SDDS)

In drug designing and manufacturing, beyond biological activity and toxicity of compound, there are several other items that have to be taken under consideration. The desired feature of biologically active substance is its water solubility, which allows easy administration. The other important issue is the interaction of drug molecules with cell membrane. All biological membranes are built of lipid bilayer which is barrier impermeable to most water-soluble (hydrophilic) molecules. This is called drug resistance and it is the major limitation for drug application. The other problem is fact that drugs permeate almost equally into diseased and health cells, what causes sides effects of treatment. For these reasons, designing of new smart drug delivery systems (SDDS) able to release entrapped biologically active compounds at the appropriate time and site of action is of great importance.

The main goal of this project is development of new systems for targeted delivery of biologically active compounds into diseased cells. These smart systems will be based on thermoresponsive block copolymers, i.e. copolymers that exhibit a critical solution temperature at which the polymer undergoes a phase change within a small temperature range. If the concentration of the polymer is increased above the CMC (critical micelle concentration) micelles (structures resembling sunflowers) with entrapped drug molecules are formed. After administration of such micelles into the body temperature rises and above the critical level the outer shell collapses and the drug can migrate out of the polymer.

Additionally, designed polymeric chains will have biologically active molecules in their structure or at their ends. This compounds are for instance: cholesterol, folic acid and ceragenin CSA-13. Steroidal skeleton of cholesterol will improve penetration of drugs into cells. Folic acid receptors are over expressed in many malignant cells and for this reason folic acid derivatives are investigated as anticancer drugs targeting molecules. In turn, CSA-13 is a new antibiotic with high affinity to negatively charged cell membranes of certain kinds of bacteria. These compounds due to their properties and/or biological activity will play an important role in targeted drug delivery.

All synthesized systems will be investigated in terms of their antibacterial, antifungal and antineoplastic properties. It is expected that these newly designed smart drug delivery systems with encapsulated active compounds will exhibit excellent therapeutic properties.