

Every single woman can suffer from gynaecological problems, very often as severe as cervix cancer. Currently available vaginal pharmacological therapies, however, are often ineffective. They are commonly based on suppository, which are very often inconvenient in use and from which a drug is released in the uncontrolled manner. Such poorly efficient therapies are cost ineffective and can substantially prolong disease period, leading, in severe cases, to drug resistance or even to patient's death.

Hydrogels, i.e. water-swollen cross-linked polymer networks, appear to be a good candidate as drug/hormone carrier in the gynecological therapies. Poor solubility in water of some drugs, however, is a major challenge for their encapsulation within the hydrogel. Apart from drug solubility the hydrogel should assure proper diffusivity of drug molecules and release profile. It should also show proper rheological characteristics that allow its facile application.

The aim of these projects is to synthesize novel hydrogel systems which can be used for delivery of hydrophobic drugs used in gynecological treatment will be encapsulated. To assure desired processability, mechanical and drug transport properties to our gels, we will synthesize dynamically cross-linked networks. Dynamic hydrogel's properties can be tailored to given application by adjusting the strength and the lifetime of network tie-points. These are dependent though, on the structure of used polymer, its concentration, the type of cross-linking interaction, etc.

As a main polymer component we will use a biocompatible polyglycidol of hyperbranched, spherical architecture (HbPLG). We will exploit this structure, by modifying the core of HbPGL with hydrophobic molecules, which will increase the affinity HbPGL to hydrophobic drug molecules. In consequence it will allow us to encapsulate a substantial amount of hydrophobic drugs, including antibiotics, hormones and anticancer drugs, within hydrogel without. At the same time, HbPGL corona with multiple diol groups will keep polymer molecules with encapsulated drug water soluble. These groups will be also used for gel cross-linking by reversible esterification.

Specific boronic polyacids will be chosen, which are able to react with HbPLG's peripheral diol groups in physiological pH of vagina. Due to reversible character of this reaction and its quick rate, formed gels will not have a fixed form but will be pliable. Such gels flow and can be easily applied onto diseased area. Moreover, dynamically crosslinked gels rebuild their structure once damaged, which assures proper coverage of a surface with a continuous gel layer. In addition the cross-linking reaction is temperature sensitive. It allows the design of systems which release drugs with rate dependent on the body temperature. For example model drug molecules can be released during inflammation.

As the output of the project we will demonstrate correlation between the structure and properties of gel-forming polymers and hydrogel properties important in a view of controlled vaginal drug delivery, such as rheological properties, drug diffusivity, encapsulation efficiency, and biocompatibility. The results will form a basis for a design of novel, efficient pharmacological formulations tailor for a given medical condition, which are also convenient for patients.