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Intermolecular interactions analysis in thermo-responsive polymer gels based on poly(2-(2-methoxyethoxy)ethyl methacrylate)

High water content makes hydrogels biocompatible and very promising material in biomedical applications like contact lenses, dressings or smart drug delivery carriers. Thermo-responsive hydrogels seem to be particularly attractive for this last purpose because they can enable precise control over the dose, release rate and delivery point of drugs. It relates to the reversible volume phase transition (VPT). A temperature raising above T_{VPT} results in rapid phase separation and release of hydrogel content. Apart from water, hydrogels can store a biologically active agent and VPT can be a trigger to drug release from such gel. The knowledge of the molecular interactions between polymer, water and drug is indispensable to use thermo-responsive hydrogels as drug delivery systems.

The main aims of presented dissertation is to learn about a nature of intermolecular interactions in three-component systems polymer-water-biologically active agent and to define the influence of polymer network architecture and selected drugs (sodium salts of ibuprofen, salicylate and naproxen which belong to the group of non-steroidal anti-inflammatory drugs were chosen) on VPT in systems based on poly(2-(2-methoxyethoxy)ethyl methacrylate) ($PMEO_2MA$).

In the bibliographic part of the dissertation the basic issues concerning aqueous polymer systems as well as the current state of knowledge on the factors determining the properties of thermo-responsive hydrogels are included. The aim of dissertation was formed on the basis of this critical review. Experimental part contains synthesis and sample preparation process as well as applied methods of research. Next, the most important chapters report results of performed studies, which were discussed in the light of literature data, and conclusions.

Raman spectroscopy was the main technique of research. These studies were performed on two-component systems polymer-water and water-drug and three-component systems. Hydrogels differing on network regularity and morphology were compared. Types of water in hydrogel and amount of water molecules hydrating single mer were distinguished and estimated. It was found that

both, total bound water surrounding the polymer chains (~11 H_2O per MEO_2MA mer) and accessibility of C=O groups for water molecules, are independent of topology of $PMEO_2MA$ network. Contrarily, network architecture strongly influences C=O – water complex stability, what is in good correlation with VPT temperature.

Also, gradient $PMEO_2MA$ hydrogels were obtained by one-step radiation-induced crosslinking polymerization method. Spectroscopic (Raman and NMR), imaging (SEM), goniometric and gravimetric techniques were used to characterize them. The results indicated that the soft, highly swelled part of the gel, is significantly more hydrophilic and exhibit more homogenous structure in microscale in comparison with the hard part of the gel. Differences at the macroscopic and molecular levels are due to post polymerization effect.

$PMEO_2MA$ hydrogels were used as model systems to study the influence of encapsulated drugs on the temperature and dynamic of the VPT. Both thermo-optical analysis and differential scanning calorimetry have shown that the VPT becomes broader and shifts towards higher temperatures with increasing drug concentration. Slowing down and magnitude of T_{VPT} shift depend on chemical structure of drug but Raman spectroscopy revealed it is not related to direct interactions between polymer and drug. Three steps of VPT in $PMEO_2MA$ gels were also distinguished and used to propose its mechanism.

Gravimetrical and UV-Vis spectrophotometric methods were used to test hydrogels for their swelling properties and ability to drug absorption. In general, the degrees of hydrogel swelling at equilibrium state (DS_{eq}) in solutions of ibuprofen, naproxen and salicylate sodium salts were greater than DS_{eq} in water and they increased for higher drug concentration. These data are opposite to DS_{eq} in solution of low molecular weight sodium salts like NaCl. The partition coefficients of mentioned drugs were estimated as greater than 1 for ibuprofen and naproxen and they are almost independent of the initial drug concentration over the investigated concentration range. The UV-Vis studies showed that rate of drug release slightly increases with temperature and VPT is a trigger significantly accelerating this process. Drug release rate is maximal at temperature near T_{VPT} and then decreases with temperature. It is probably due to formation of skin layer – outer impermeable shell of polymer network becoming hydrophobic because of high ambient temperature.

Key words: thermo-responsive hydrogels, Raman spectroscopy, intermolecular interactions, Volume Phase Transition, drug delivery systems

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