In many clinical studies it has already been demonstrated that higher efficiency of APIs (active pharmaceutical ingredients) signifi- cantly reduces menace of many diseases. API has higher efficiency when has good bioavailability and that is good solubility in human fluids and good permeability in gastrointestinal tract (GIT). Based on this pharmacoceutical properties of API Food and Drug Administration (FDA) created the Biopharmaceutical Classification System (BCS). BCS is based on aqueous solubility and intestinal permeability of the drug substance in human. It classifies API into one of four classes.

The Biopharmaceutical Classification System (BCS)

The highly soluble API – when the highest oral dose is soluble in ≤ 250 ml of aqueous media over the pH range of 4.0 to 6.8.

The highly permeable API – when the highest oral dose is absorb of >50% in GIT.

Unfortunately a lot of pharmaceutical substances exhibit low bioavailability and solubility in water. That is why current pharmaceutical research focuses on increasing solubility and thus also bioavailability of these substances.

API-polymer systems

In our work we focused our attention on the study of structural properties of APIs in the prepared solid polymer dispersions, solutions and co-crystals exhibiting increased solubility. Nowadays we are testing properties of acetylsalicylic acid (AcSalAc) as an API system with relatively low solubility. One of several procedures of creating bioavailable system – lyophilization (lyo), was used to combine this API with polymeric non-toxic, water-soluble matrix – polyvinylpyrrolidone (PVP), polyvinyl-2-hydroxypropylmetacrylamide) (HPMA), poly(2-ethyl-2-oxazoline) (PEO) and polyethylene glycol (PEG). The polymers were used with different molecular weight. As a solvents of this API-polymer system we used non-toxic and biodegradable compounds, which solubilize API and polymer matrix as water, ethanol and tert-butanol (T-but).

Samples of API-polymer system:
- Sample A: AcSalAc/ T-but, 30% + PEO/water, 70%.
- Sample B: AcSalAc/ T-but, 30% + PVP/water, 70%.
- Sample C: AcSalAc/ T-but, 30% + HPMA/water, 70%.
- Sample D: AcSalAc/ T-but, 30% + PEO/water, 50% + PVP/water, 50%.
- Sample E: AcSalAc/ T-but, 30% + PEO/water, 70%.
- Sample F: AcSalAc/ T-but, 30% + PEO/water, 70%.

The creation of homogeneous solid dispersions, consisting of AcSalAc dispersed in various polymer matrices, is confirmed by the identical value of T1 (τ1) relaxation. The AcSalAc molecule adopted high frequency motion of polymer in measured samples of the solid dispersions (short τ1(τ1)).

Relaxation experiments of samples and particular components

The API-polymer systems of acetylsalicylic acid (API) in combination with PEG, PVP, PEO or HPMA (polymeric matrix) were prepared by lyophilization. The polymers were used with different molecular weight. The structural reason observed in polymer-drug interaction were probed by a wide range of 1H CP/MAS NMR, 13C MAS NMR, 19F DQ-BABA and relaxation experiments. It was confirmed that lyophilization of the solutions consisting of AcSalAc (30%) /T-but with PVP (70%) / T-but or PEG (70%) / water leads to the formation of the required amorphous solid solutions, the solution consisting of AcSalAc (30%) / T-but with HPMA (70%) / water leads to the formation of the interstitial nanocrystalline dispersion and the solution consisting of AcSalAc (30%) / T-but with PEG (70%) / T-but leads to the formation of the crystalline solid dispersion.

This statement follows from dramatic broadening of NMR signals of AcSalAc in 1H CP/MAS NMR spectrum and changes in τ1 relaxation times. In dispersions with PEG the new signal of the CH group is observed. The decrease in value of the τ1(τ1) relaxation times of the AcSalAc in samples confirms molecular mixing API with polymer. The correlation between API and polymer matrix in samples D is shown in the 19F DQ-BABA experiments. We managed to prepare API-polymer systems with expectation of creation of the amorphous solid solutions and solid dispersions. This and other systems will be subject of the incoming studies by advanced ssNMR experiments, Raman spectroscopy, dissolution profile...