ABSTRACT

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Title of Thesis **Modification of Physico-Chemical Properties of Biologically Active Compounds**

The majority of newly developed biologically active compounds (API) belong to the 2. – 4. BCS class, i.e. groups that have problematic permeability and/or solubility. This work deals with modifications of the physico-chemical properties of model biologically active substances.

The first group selected for these modifications were bisphosphonates – ibandronate and risedronate. By using a rational selection of co-crystallisation partners, co-crystals of model APIs were prepared with co-crystallisation partners from the group of monosaccharides and their derivatives. Available solid state analytical methods – NIR, Raman spectroscopy, ^{31}P CP/MAS NMR – were used for the characterization of the resulting cocrystal(s), and in the case of co-crystals of risedronate salt, ^{13}C CP/MAS NMR, XRPD and DSC were used. There was only one positive sample among all the prepared samples of co-crystals of ibandronate salt, and that was with the use of phenyl-β-D-galactopyranoside as a co-crystallisation partner. PAMPA experiments were undertaken to evaluate its permeability. It unfortunately failed to prove the assumption that the prepared co-crystal would had a higher permeability than the used standards. Experiments involving risedronate unfortunately did not provide the desired result, but it was managed to prepare a new polymorph of risedronate.

The second group consisted of steroid compounds, angiotensin II receptor antagonists (ARBs, sartans) and alaptid. Focus was aimed at the formation of complexes with higher solubility than the parent APIs. It was prepared and by means of NIR and Raman spectroscopy characterized tens of successfully created new entities with improved solubility. It was proved, that in the case of steroid substances, the capability of releasing of the API in higher pH; the complex API – excipient was stable at low pH values, thus it provided the targeted release in the intestine. Alaptid water-solubity was to be increased by formation of nanosuspension and preparation of stable complexes of alaptid with conventional excipients. Prepared nanoparticles were characterised by NANOPHOX device and the obtained complexes with much higher water-solubility were characterized by NIR. Further, it was investigated the possibility to affect the penetration through membranes. PAMPA experiments shown better penetration abilities of both nanosuspension and some complexes of alaptid – excipient. On the contrary, experiment with Franz diffusion cell shown that the complexes API –excipient penetrates through skin much better then both micronized and nanosized alaptid. Modification of penetration was also evaluated from topical pharmaceutical compositions and extreme effect of used *vehiculum* was discovered.