SUMMARY

There are several different approaches for high performance liquid chromatography method development. Beside traditional approach »trial and error«, different software programs for method development and optimization are available, which are based on different retention models. Main goal of my PhD work was application of solvatic model for prediction of retention at gradient elution in reversed-phase liquid chromatography with different type of stationary phases (C18, C8 and phenyl-hexyl) and with different type of mobile phases (classical aqueous mobile phases – phosphoric acid/ammonium acetate and more modern aqueous mobile phases – ionic liquids) for active pharmaceutical ingredient aripiprazole and its related substances, described in European Pharmacopoeia. As this compounds have very similar chemical structure, their separation is challenging. Retention prediction was suitable on all examined stationary phases with 0.1 % phosphoric acid / 10 mM ammonium acetate/ 1 mM ionic liquid [BMIM][BF_4] as aqueous mobile phases and acetonitrile / methanol as organic modifiers. Predicted retention take into account structural formulae of compounds and properties of stationary and mobile phases. In the case of classical mobile phases the average difference between experimental and predicted retention times was -14 – -17 % on phenyl-hexyl stationary phase, where the highest matching was obtained. After utilisation of the solvation retention model with data from one experimental run, the average difference decreased to maximal -7 % and after contribution of data from two experimental runs, to maximal -2 % on all examined stationary phases (for majority of studied compounds difference between predicted and experimental values is lower than -3 %). The influence of classical and modern aqueous mobile phases on resolution of individual components and simmetry factor was evaluated. At experimental work three different ionic liquids were examined. Ionic liquid [BMIM][BF_4] was the most appropriate and the most useful. In the case of usage of modern mobile phases (ionic liquids) and after utilisation of the solvation retention models with data from one experimental run, the average difference decreased to maximal -5 % and after contribution of data from two experimental runs, to maximal -1 %. In the case of ionic liquid [BMIM][BF_4] in comparison with buffer ammonium acetate, chromatographic peaks were more symmetrical. The stability of aripiprazole at higher temperatures and at oxidation conditions was studied. Degradation products of aripiprazole were identified with mass spectrometry coupled to liquid chromatography. Beside pharmacopoeia impurity two additional degradation products were identified.