

ABSTRACT

Charles University, Faculty of Pharmacy in Hradec Králové

Department of Pharmaceutical Chemistry and Pharmaceutical Analysis

Candidate **Mgr. Tomáš Nejedlý**

Supervisor **prof. RNDr. Jiří Klimeš, CSc.**

Title of Doctoral Thesis **Development of HPLC methods for analytical evaluation of drug products and model studies of natural degradation of drug residues**

The presented doctoral thesis describes two areas of pharmaceutical analysis. The first part is focused on development of validated chromatographic methods for pharmaceutical-analytical assesment of drug products and their rutine use in quality control laboratories. The second part deals with the very actual topic of environmental analysis and residues of pharmaceutical substances in sewage and surface water.

The first developed method is suitable for quality evaluation of cream dosage forms containing aciclovir active substance. This method is suitable for assay of active substance and its three related substances. In addition it is validated for assay of preservatives contained in cream base. The second chromatographic method is developed for determination of tablets containing 1 mg of risperidone antipsychotic drug per tablet. This method was validated for active substance assay and the four mostimportant pharmacopoeial impurities. The last method is focused on analytical evaluation of oral drops solution containing sodium picosulfate and sodium benzoate preservative. This method is validated for assay of active substance, presevative and two main degradation products. Modern Ultra-Highperformance chromatographic conditions and instrumentation including UHPLC columns packed with sub 2 μm particles were used for all three methods. The aim of these studies was to shorten the time needed for single analysis and to significantly reduce the volume of used organic solvents. All validation parameters results are compliant with ICH and SÚKL requirements and guidelines.

Environmental analytical part of this disertation thesis is focused on creation of laboratory model for natural degradation of pharmaceuticals in surface water. This pilot study describes the model of natural degradationof estrogen hormone drug 17- α -ethinylestradiol as a signifiant contaminant of environment. The active substance was exposed to light, temperature and oxidation stress conditions determined by the ICH guidelines for stability testing. The kinetic parameters of rate degradation were evaluated afterwards. Another aim of this study was to identify the breakdown products of photodegradation processes in water matrices by means of GC/EI-MS method. Total organic carbon concentration was observed during the experiments and a signifiant decrease of its value was found in photo-oxidative testing. The model surface and salt water media were used and compared with samples of natural surface water. This disertation thesis provides comprehensive and complex data for stability of 17- α -ethinylestradiol in environment.