Abstract (EN)

In the first part of this work, analytical methods for determination of impurities of active pharmaceutical ingredients (API) in combined pharmaceutical dosage forms were developed and validated. Development of the methods covered both the optimization of sample preparation procedure and chromatographic conditions. The methods were validated according to International Conference on Harmonization guideline and both of them were confirmed to be able to analyze stability samples. Impurities in paracetamol, codeine phosphate hemihydrate and pitophenone hydrochloride in the presence of fourth API fenpiverinium bromide were separated by using ion-pair reversed phase chromatography with gradient elution. Symmetry C_{18}, 250 x 4,6 mm, 5 μm heated to 35 °C was used as a separation column. A diode array detector was used. The detection wavelengths were set as follows: 220 nm for paracetamol impurity K, 245 nm for paracetamol and its other impurities and 285 nm for codeine, pitophenone and their impurities. Impurities in valsartan, amlodipine besylate and hydrochlorothiazide were separated by reversed phase UHPLC method with gradient elution. Chromatographic column Zorbax Eclipse C_8 RRHD, 100 x 3,0 mm, 1,8 μm heated to 30 °C and spectrophotometric detection were used. The detection wavelengths were set as follows: 225 nm for valsartan, its impurities and for impurity D of amlodipine besylate, 360 nm and 271 nm for amlodipine, respectively hydrochlorothiazide and their impurities.

In the second part of this work, thin-layer monolithic stationary phases were prepared on a glass holder. Polymerization mixtures contained glycidyl-methacrylate and 2-hydroxyethyl-methacrylate (monomers), ethyleneglycol-dimethacrylate (cross-linker), decan-1-ol, cyclohexan-1-ol, propan-1-ol and butan-1,4-diol (porogens) in different ratios and 2,2-dimethoxy-2-phenyl-acetophenone as an initiator. Monolithic layers were prepared in-situ (UV initiation, 254 nm) between plexiglass and silanized glass layers separated by teflon gasket with defined thickness of 25, 50, 76 and 127 μm. The main examined characteristic of the monolithic layers were their mechanical stability and speed of capillary action of hexane depending on composition of polymerization mixture. The selected monolithic layer was tested as a stationary phase for mass detection with desorption atmospheric pressure photoionization (DAPPI).