Abstract

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Title of Diploma Thesis: Optimization and validation of UHPSFC-UV methods for quality control of agomelatin and atorvastatin in drug substance and in tablets

The aim of this master thesis was to develop two ultra-high performance supercritical fluid chromatography (UHPSFC) methods with PDA detection for determination of agomelatine and atorvastatin and its potential impurities. UHPSFC system Acquity UPC^2 with PDA detector was used for measurement.

The separation of agomelatine was performed by Torus Diol column (100 × 3.0 mm, 1.7 µm). Gradient elution was performed using CO_2 with the mixture of methanol/acetonitrile (1:1) and 31.5 mM (0,1 %) ammonium hydroxide as a mobile phase. Column temperature was set at 40 °C and BPR (back pressure regulator) pressure at 2000 psi. The detection wavelength was set at 225 nm. The method was developed for measurment of API (active pharmaceutical ingredient) and subsequently for tablets.

The separation of atorvastatin was performed using Acquity UPLC HSS C18 SB column (100 × 3.0 mm, 1.8 µm). Gradient elution was performed using CO_2 with the mixture of methanol/ acetonitrile (2:1), 15 mM formic acid, 2.5 mM ammonium hydroxide and 5 % water as a mobile phase. Column temperature was set at 45 °C and BPR pressure at 2000 psi. The detection wavelength was set at 244 nm. The method was developed for measurement of API.

Both methods were validated according to the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) quality guidelines including linearity, accuracy, precision and interday accuracy and precision. Method accuracy was in the range of 95 - 105 % and precision expressed as a relative standard deviation RSD ≤ 5 % in both methods.

Keywords: agomelatine; atorvastatin; method development; UHPSFC; PDA detector; validation; quality control; impurities