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A new, rapid, stability-indicating UPLC method for separation and determination of impurities in amlodipine besylate, valsartan and hydrochlorothiazide in their combined tablet dosage form

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Abstract

A new rapid stability-indicating UPLC method for separation and determination of impurities in amlodipine besylate, valsartan and hydrochlorothiazide in their combined tablet dosage form was developed. The separation of Ph. Eur. related substances of amlodipine besylate (A, B, D, E, F, G), hydrochlorothiazide (A, B, C), valsartan (B, C), two other valsartan impurities (S)-2-(N-{[2'-cyanobiphenyl-4-yl]methyl}pentanamido)-3-methylbutanoic acid and (S)-3-methyl-2-{[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methylamino}butanoic acid and several unknown impurities was achieved by reversed phase liquid chromatography with UV detection. The detection wavelengths were set as follows: 225 nm for valsartan, its impurities and for the impurity D of amlodipine, 271 nm for hydrochlorothiazide and its impurities and 360 nm for amlodipine and its impurities except for impurity D. Zorbax Eclipse C8 RRHD (100 x 3.0 mm, 1.8 μm) was used as a separation column and the analytes were eluted within 11 minutes by a programmed gradient mixture of 0.01M phosphate buffer pH 2.5 and acetonitrile. The method was successfully validated in accordance to the International Conference of Harmonization (ICH) guidelines for amlodipine besylate and its impurity D,