Synchronized Stability Indicating RP-LC Methods for Determination of Metolazone with Losartan Potassiumor Spironolactone in Presence of Their Degradation Products

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Abstract

Two precise and selective stability-indicating RP-LC methods have been developed and validatedfor simultaneous determination of metolazone in its binary mixture with losartan potassium(method 1) and spironolactone (method 2) in the presence of their degradation products. Formethod 1, the chromatographic separation was achieved on Kromasil C18column, the mobilephase consisted of a mixture of 0.1% ortho-phosphoric acid in acetonitrile and 0.1% ortho-phos-phoric acid in water (28:72, v/v) pumped at flow rate 2 mL/min and UV detection at 235nm.Linearity was determined over the concentration range of 2ï16mg/mL for metolazone and40ï320mg/mL for losartan potassium. For method 2, chromatographic separation of metolazoneand spironolactone was achieved on a Symmetry C8column using a mobile phase that consistedof acetonitrile, methanol, and 0.1% ortho-phosphoric in water in gradient mode pumped at a flowrate 1.5 mL/min with programed wavelength detection. Linearity was determined over the concen-tration range of 2ï16mg/mL for metolazone and 20ï160mg/mL for spironolactone. The suggestedmethods were proved to be highly selective, precise and accurate for simultaneous determinationof the cited drugs in their combined pharmaceutical dosage form in the presence of their degrad-ation products. The proposed methods were validated in compliance with ICH guidelines.

Journal of liquid chromatography and related techniques 2020, February