Research article

A Fast, Stability-Indicating, and Validated Liquid Chromatography Method for the Purity Control of Lercanidipine Hydrochloride in Tablet Dosage Form

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Abstract

A robust, sensitive, and stability-indicating rapid resolution liquid chromatography method for the simultaneous determination of process impurities and degradation products of lercanidipine hydrochloride in pharmaceutical dosage form was developed and validated. The chromatographic separation was performed on the Zorbax SB C18 [(50 × 4.6) mm] 1.8 μm column, using gradient elution of a potassium dihydrogen phosphate buffer (pH 3.5, 0.01 M) and acetonitrile. The flow rate was 1.0 ml/min and UV detection was performed at 220 nm. The method was further evaluated for its stability-indicating capability by hydrolytic, oxidative, thermal, thermal with moisture, and photolytic degradation studies. All acceptance criteria of the International Conference on Harmonization guidelines for validation were covered in the method validation. This method can be used for purity control during manufacture and real time stability studies. A shorter run time of 10 minutes and good solution stability for at least 48 hours allowed the quantification of more than 50 samples per day with comparatively lower costs than existing methods.

Keywords

Lercanidipine • Impurities • RRLC • Stability indicating • Validation
Simultaneous Estimation of Ofloxacin and Ornidazole in Combined Dosage Forms by Dual Wavelength and Ratio Spectra Derivative Methods using UV-Spectrophotometer

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Abstract: Two sensitive, validated, accurate, precise and specific methods were developed as useful alternatives for the simultaneous quantitative estimation of Ofloxacin and Ornidazole in the combined pharmaceutical formulation. The first method was based on the first derivative of ratio ultra-visible spectra. Signal intensities at 323.0nm and 260.0nm were used in this method for Ofloxacin and Ornidazole respectively. The second method was dual wavelength method in which, 266.0nm and 287.0nm were selected for estimation of Ofloxacin and 271.0nm and 319.0nm were selected for estimation of Ornidazole. In both the methods 0.1N Hydrochloric Acid is used as diluent. Calibration curve was established in the range of 1.92 - 9.6µg/ml for Ofloxacin and 4.8 - 24.0µg/ml for Ornidazole in both the methods. Both drugs show linearity in the range and furnishing near quantitative analyte recoveries. Performance characteristics of the analytical methods were evaluated by using commercial samples and both the methods shown accurate, precision and specificity. These two validated methods are easy to apply, use relatively simple equipment, require minimum analysis time and do not use polluting reagents.

Keywords: Ofloxacin, Ornidazole, UV-Spectrophotometer, Ratio Spectra Derivative, Dual wavelength.
CHAPTER 1

INTRODUCTION
RAPID RESOLUTION LIQUID CHROMATOGRAPHY (RRLC)
UV-SPECTROPHOTOMETRIC METHODS AND THEIR APPLICATION
SUPER CRITICAL FLUID CHROMATOGRAPHY (SFC) AND ITS APPLICATION
IMPURITY PROFILING
Using
Prep HPLC
IR
LC-MS
$^1$H NMR
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ATTENDED
Determination of assay and uniformity of content of ramipril and telmisartan in their multiple dosage forms by a developed and validated supercritical fluid chromatographic technique

Saumil Mehta,* Sukhdev Singh,a Kishor Chikhalia,a Priti Mehta and Tejas Dadhaniab

Considered a leading “green” separation technology, supercritical fluid chromatography (SFC) can be the best technique to separate and estimate chemical compounds. A precise, accurate and robust supercritical fluid chromatographic method was developed and validated for the determination of assay and uniformity of content of ramipril and telmisartan in their combined dosage forms. The chromatographic separation was achieved on a Zorbax SB-Phenyl column (150 mm × 4.6 mm, 5 μm) using supercritical carbon dioxide doped with 10% v/v methanol as a modifier, at a flow rate of 2.0 mL min⁻¹. Column oven temperature was 35.0 °C, and UV detection was performed at 205 nm. The densities and polarities of the mobile phase were optimized from the effects of pressure, temperature and modifier concentration on chromatographic parameters. The developed method was validated in terms of specificity, linearity and range, accuracy, robustness and precision applying International Conference on Harmonization guidelines. The method was successfully applied for the assay and for the uniformity of content of different marketed formulations containing ramipril and telmisartan individually and in combination.

Introduction

Chemically, ramipril (RAM) is a (2S, 3aS, 6aS)-1-[((S)-N-([S]-1-carboxy-3-phenylpropyl)alanyl)octahydrocyclopenta[b]pyrrole-2-carboxylic acid, 1-ethyl ester. It is an angiotensin converting enzyme (ACE) inhibitor. The drug is used for treating blood pressure and congestive heart failure. Telmisartan (TELMi) is a 4-[[4-methyl-6-(1-methyl-2-benzimidazolyl)-2-propyl-1-benimidazolyl]-methyl]-2-biphenyl carboxylic acid used for the treatment of hypertension in patients. RAM and TELMi combinations are used to lower blood pressure, and as anti-hypertensive agents. The combinations of RAM and TELMi are commercially available as solid oral formulation in medicinally recommended ratios of 5 : 40 and 2.5 : 40 respectively. The chemical structures of RAM and TELMi are presented in Fig. 1.

In the Indian pharmacopoeia, RAM and TELMi API, RAM capsule, RAM tablet, and TELMi tablet are official. Both drugs are also official in the European pharmacopoeia and British pharmacopoeia. In the United States pharmacopoeia both drug substance, RAM capsule and TELMi tablet are official.

Many methods have been reported for the estimation of RAM and TELMi in their combined dosage form by several analytical techniques like HPLC, HPTLC, and UV spectrophotometry. However, since UV-spectroscopy is not a selective technique and HPLC consumes too much solvent, we have developed such a “green” technique, for the estimation of both drugs by SFC.

For laboratories overwhelmed with solvent disposal, time-consuming solvent cleanup, solvent cost and pollution, supercritical fluid chromatography (SFC) is a beneficial alternative to purification and analytical applications. Considered a leading

Fig. 1  Chemical structures of (A) RAM and (B) TELMi.
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