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Short communication

A validated stability-indicating UPLC method for desloratadine and its impurities in pharmaceutical dosage forms

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ABSTRACT

A novel stability-indicating gradient reverse phase ultra-performance liquid chromatographic (RP-UPLC) method was developed for the determination of purity of desloratadine in presence of its impurities and forced degradation products. The method was developed using Waters Aquity BEH C18 column with mobile phase containing a gradient mixture of solvents A and B. The eluted compounds were monitored at 280 nm. The run time was 8 min within which desloratadine and its five impurities were well separated. Desloratadine was subjected to the stress conditions of oxidative, acid, base, hydrolytic, thermal and photolytic degradation. Desloratadine was found to degrade significantly in oxidative and thermal stress conditions and stable in acid, base, hydrolytic and photolytic degradation conditions. The degradation products were well resolved from main peak and its impurities, thus proved the stability-indicating power of the method. The developed method was validated as per ICH guidelines with respect to specificity, linearity, limit of detection, limit of quantification, accuracy, precision and robustness. This method was also suitable for the assay determination of desloratadine in pharmaceutical dosage forms.

1. Introduction

Desloratadine is indicated for the relief of the nasal and non-nasal symptoms of seasonal allergic rhinitis in patients 2 years of age and older. Its chemical designation is 8-chloro-6,11-dihydro-11-(4-piperdinylidene)-5*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridine (Fig. 1). It is available as 5 mg tablets and also available as syrup.

In the literature there were limited LC methods have been reported for determination of desloratadine in pharmaceutical preparations. The assay method [1] reported describes the separation of degradation impurities from deslaratadine formed through forced degradation studies, but it was out of scope because it did not separate and determine the impurities. A validated RP-HPLC method has been reported for quantification of desloratadine in pharmaceutical forms [2], a spectophotometric, spectrofluorometric and HPLC method has been reported for determination desloratadine in dosage forms and in human plasma [3] and a LC method has been reported for simultaneous determination of loratadine and desloratadine in pharmaceutical preparations using micro-emulsion as eluent [4], but forced degradation study and impurity details were not reported in these articles [2–4]. We have developed a stability-indicating RP-LC method that can separate and determine deslaratadine and its five impurities namely imp-A, imp-B, imp-C, imp-D and imp-E (Fig. 1).

Ultra-performance liquid chromatography (UPLC) is a recent technique in liquid chromatography, which enables significant reductions in separation time and solvent consumption. Literature indicates that UPLC system allows about ninefold decreases in analysis time as compared to the conventional HPLC system using 5 μm particle size analytical columns, and about threefold decrease in analysis time in comparison with 3 μm particle size analytical columns without compromise on overall separation [5–9].

Hence a rapid simple reproducible gradient stability-indicating RP-UPLC method was developed and validated for the quantitative determination of desloratadine and its five impurities in pharmaceutical dosage forms.

2. Experimental

2.1. Chemicals and reagents

The purity of all chemicals was above 98%. Tablets and standards of desloratadine (99.8%) and its five impurities namely imp-A (98.2%), imp-B (99.1%), imp-C (98.1%), imp-D (98.9%) and imp-E (99.5%) were supplied by Dr. Reddy's laboratories limited, Hyderabad, India. The HPLC grade acetonitrile, methanol, tertahydrofuran

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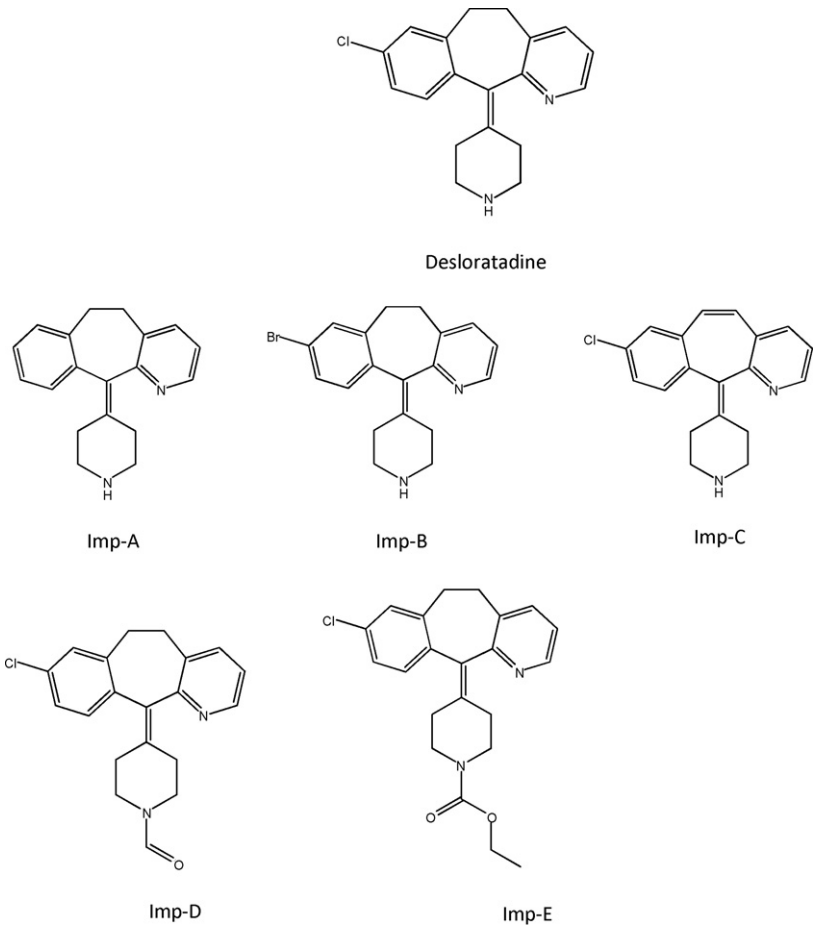

Fig. 1. Structures of desloratadine and its five impurities.

and analytical grade KH_2PO_4 and ortho phosphoric acid were purchased from Merck, Darmstadt, Germany. High purity water was prepared by using Milli Q Plus water purification system (Millipore, Milford, MA, USA).

2.2. Equipment

Acquity UPLC™ system (Waters, Milford, USA) we used consists of a binary solvent manager, a sample manager and a photodiode array (PDA) detector. The output signal was monitored and processed using empower2 software. Cintex digital water bath was used for hydrolysis studies. Photostability studies were carried out in a photostability chamber (Sanyo, Leicestershire, UK). Thermal stability studies were performed in a dry air oven (Cintex, Mumbai, India). The pH of the solutions was measured by a pH meter (Thermo Orion Model 420 A, USA). All solutions were degassed by ultra sonication (Power sonic 420, Labtech, Korea) and filtered through a 0.45 μm Nylon 66 filter (PALL Life Sciences, USA). Intermediate precision was performed on different Acquity UPLC™ system (Waters, Milford, USA) consists of a binary solvent manager, a sample manager and a tunable ultraviolet (TUV) detector.

2.3. Chromatographic conditions

The method was developed using Waters Aquity BEH C18, 50 mm × 2.1 mm; 1.7 μm column (Waters, Milford, USA) with mobile phase containing a gradient mixture of solvents A and B. 0.01 M potassium dihydrogen orthophosphate buffer, pH adjusted to 2.5 with orthophosphoric acid was used as buffer. Buffer, methanol and acetonitrile in the ratio 80:15:5, v/v/v; was used as solvent A and buffer, tetrahydrofuran and acetonitrile in the ratio 30:5:70, v/v/v; was used as solvent B. The gradient program (T/%B) was set as 0/0, 1.5/0, 5.5/80, 6.5/80, 7.0/0 and 8.0/0. The mobile phase was filtered through a nylon 0.45 μm membrane filter. The flow rate of the mobile phase was 0.6 ml/min. The column temperature was maintained at 30 °C and the wavelength was monitored at 280 nm. The injection volume was 5 μl.

2.4. LC–MS/MS conditions

LC–MS/MS system (Waters 2695 Alliance liquid chromatograph coupled with quattromicro mass spectrometer with Mass Lynx software, Waters Corporation, Milford, USA) was used for the unknown compounds formed during forced degradation studies. Hypersil BDS C18, 250 mm × 4.6 mm, 5 μm column (Thermo Scientific, USA) was used as stationary phase. 0.01 M ammonium formate (Merck, Darmstadt, Germany) was used as buffer. Buffer, methanol and acetonitrile in the ratio 80:15:5, v/v/v; was used as solvent A and buffer and acetonitrile in the ratio 25:75, v/v/v; was used as solvent B. The gradient program (T/% solvent B) was set as 0/0, 10/0, 40/80, 50/80, 52/0 and 60/5. Solvent A was used as diluent. The flow rate was 1.0 ml/min. The analysis was performed in positive electro spray positive ionization mode. Capillary and cone voltages were 3.5 kV and 25 V, respectively. Source and dissolvation temperatures were 120 and 350 °C, respectively. Dissolvation gas flow was 650 l h^{-1}.

2.5. Preparation of stock solutions

A stock solution of desloratidine (1.0 mg/ml) was prepared by dissolving appropriate amount of drug in the solvent A. Working