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Journal of Pharmaceutical and Biomedical Analysis 38 (2005) 355–359
JOURNAL OF PHARMACEUTICAL AND BIOMEDICAL ANALYSIS
www.elsevier.com/locate/jpba

Short communication

Determination of desloratadine in drug substance and pharmaceutical preparations by liquid chromatography

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Received 29 August 2004; received in revised form 1 January 2005; accepted 4 January 2005
Available online 9 February 2005

Abstract

A simple and selective LC method is described for the determination of desloratadine in drug substance and pharmaceutical preparations. Chromatographic separation was achieved on a Diamonsil BDS C_{18} column using a mobile phase of a mixture of methanol, 0.03 mol/l heptanesulphonic acid sodium and glacial acetic acid (70:30:4, v/v) at a flow rate of 1.0 ml/min with detection at 247 nm. The developed method was validated in terms of selectivity, linearity, limit of quantitation, precision, accuracy and solution stability. The proposed LC method achieved satisfactory resolution between desloratadine and loratadine possibly present in desloratadine drug substance and other impurities in the mother liquor of the synthetic process. It can be used for the synthetic process control and determination of desloratadine in drug substance and pharmaceutical preparations.

Keywords: Desloratadine; Liquid chromatography; Drug substance; Pharmaceutical preparations

1. Introduction

Desloratadine (Fig. 1, also called descarboethoxyloratadine), an orally active major metabolite of non-sedating H1-antihistamine loratadine, is a highly selective peripheral H1 receptor antagonist that is significantly more potent than loratadine and has an excellent overall pharmacological profile [1–4].

Several analytical methods were available for the determination of desloratadine, which involved gas chromatography with nitrogen–phosphorus detection [5], liquid chromatography with fluorescence detection (LC) [6–7], ultraviolet detection [8] or mass spectrometric detection [9–11]. However, all of these methods were developed for determination of desloratadine in biological samples and applied for pharmacokinetic studies. For quality control of pharmaceuticals, LC methods with ultraviolet detection are often preferred in ordinary laboratories. No LC methods with ultraviolet detection were available for simultaneous determination of desloratadine and its related substances including loratadine in drug substance and pharmaceutical preparations. Desloratadine was synthesized by the hydrolytic decarboxylation of loratadine, which may be contained in the final product due to the incomplete reaction and final purification. Therefore, it was necessary to develop a simple and selective LC method for the development of desloratadine and its pharmaceutical preparations.

The aim of this work was to develop an LC method with ultraviolet detection for the simultaneous determination of desloratadine and loratadine in desloratadine drug substance and pharmaceutical preparations. The present LC method was validated following the ICH guidelines [12,13].

2. Experimental

2.1. Chemicals and reagents

Desloratadine reference standard (purity of 99.8%) and tablets were from Shenyang Pharmtech Institute of Pharmaceuticals (Shenyang, China). Each tablet contains 5 mg

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doi:10.1016/j.jpba.2005.01.003

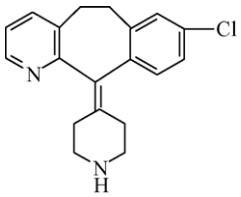

Fig. 1. Chemical structure of desloratadine.

desloratadine. LC-grade methanol and heptanesulphonic acid sodium (HAS) were used. All other chemicals and reagents used were of analytical grade unless indicated otherwise.

2.2. Apparatus and chromatographic conditions

Chromatographic separation was performed on an Agilent 1100 liquid chromatographic system equipped with a G1310A pump, a variable UV/vis detector, a G1328A manual injector with a 20 μl loop (Agilent, USA). EChrom 98 chromatography workstation was applied for data collecting and processing (Elite, China). A Shimadzu UV-2201 UV/vis double-beam spectrophotometer (Shimadzu, Japan) was used for scanning and selecting the detection wavelength.

A Diamonsil BDS C_{18} column (150 mm × 5.0 mm, 5 μm) was used for the separation. Mobile phase of a mixture of methanol, 0.03 mol/l HAS and glacial acetic acid (70:30:4, v/v) was delivered at a flow rate of 1.0 ml/min with detection at 247 nm. The mobile phase was filtered through a 0.45 μm membrane filter and degassed. The injection volume was 20 μl. Analysis was performed at ambient temperature.

2.3. Preparation of standard solutions

A stock solution with desloratadine at about 100 μg/ml was prepared with mobile phase. Standard solutions were prepared by dilution of the stock solution with mobile phase to give solutions containing desloratadine over the concentration range from 5.0 to 50.0 μg/ml.

2.4. Preparation of degraded samples for selectivity study

Forcedly degraded tablet samples under different stress conditions (heat, light, acid and base) were prepared for the evaluation of the selectivity of the developed LC method. For thermal degradation, the tablet sample (100 mg) was placed into a test tube and heated over a Bunsen flame for 2 min and then cooled to room temperature. The degraded sample was dissolved with mobile phase and transferred into a 25 ml volumetric flask and brought to volume with mobile phase. For photodegradation, the tablet sample was placed under light (4500 lx) for 8 h and then proceeded the same as indicated for thermal degradation. For acid and base degradation, the tablet samples were individually placed into two test tubes and 3 mol/l HCl and 3 mol/l NaOH were added and heated over a Bunsen flame for 2 min and then cooled to room temperature. The degraded samples were then neutralized and transferred into 25 ml volumetric flasks and brought to volume with mobile phase. All the prepared degraded sample solutions were further diluted with mobile phase to reach a concentration within the linear range. The resulting solutions were used as the degraded sample solutions and determined under the described chromatographic conditions.

2.5. Preparation of sample solutions for assay

Twenty tablets were accurately weighed and finely powdered. An accurately weighed portion of the powder equivalent to 50 mg of desloratadine was transferred to a 25 ml volumetric flask. After about 10 ml of mobile phase was added, the mixture was shaken well and brought to volume with mobile phase, and filtered. The first 10 ml of the filtrate was rejected, and 1 ml of the subsequent filtrate was quantitatively transferred to a 100 ml volumetric flask and brought to volume with mobile phase. The resulting solution was used as the sample solution for assay and determined under the described chromatographic conditions.

3. Results and discussion

3.1. Method development

In this work, a C18 column was used for the chromatographic separation. Our attention was mainly focused on the optimization of the rest chromatographic conditions such as the components and ratio of mobile phase, flow rate and detection wavelength. Our initial tests showed that compared with loratadine, desloratadine displayed a larger polarity and less retention on the column. It was suggested that a mobile phase containing ion-pairing reagent at acidic pH value might favor the retention of desloratadine on the column to achieve a reasonable retention and resolution between the two drugs. After initial attempts, heptanesulfonic acid sodium (HAS), methanol and glacial acidic acid became the components of mobile phase. Afterwards, the molar concentration of HAS and the ratios of the components in mobile phase were further optimized. After several trials a mixture of methanol, 0.03 mol/l HAS and glacial acidic acid (70:30:4, v/v) with a flow rate at 1.0 ml/min was finally adopted. Since desloratadine in the mobile phase exhibits maximum absorption at 247 nm, thus the wavelength 247 nm was chosen for detection. The described chromatographic conditions achieved satisfactory resolution, reasonable retention and symmetric peak shapes for desloratadine and its related substances including loratadine, under which the retention times were 5.4 min for desloratadine and 7.4 min for loratadine, respectively, and the run time was less than 10 min.