

Short communication

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

Meiling Qi^{a,*}, Peng Wang^b, Yingshu Geng^b

^a Department of Chemistry, School of Science, Beijing Institute of Technology, Beijing 100081, China

^b Shenyang Pharmtech Institute of Pharmaceuticals, Shenyang 110016, China

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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 C₁₈ 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.

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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 deslo-

ratadine 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

* Corresponding author. Tel.: +86 1068912667; fax: +86 1068913293.
E-mail address: mlqi@bit.edu.cn (M. Qi).

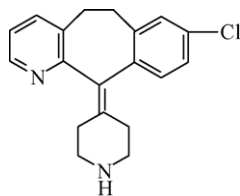


Fig. 1. Chemical structure of desloratadine.

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 μ l 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 C₁₈ column (150 mm \times 5.0 mm, 5 μ m) 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 μ m membrane filter and degassed. The injection volume was 20 μ l. Analysis was performed at ambient temperature.

2.3. Preparation of standard solutions

A stock solution with desloratadine at about 100 μ g/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 μ g/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, heptanesulphonic acid sodium (HAS), methanol and glacial acetic 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 acetic 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.

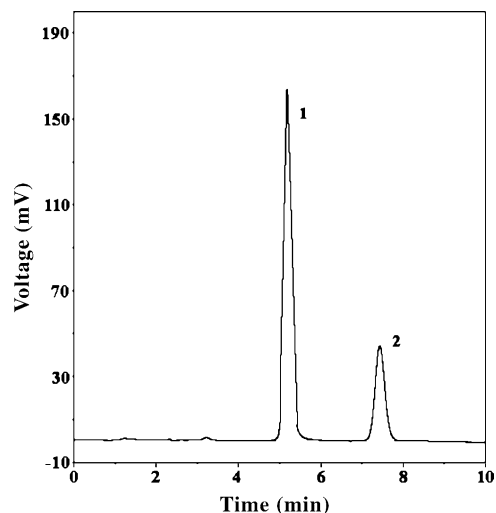


Fig. 2. LC chromatogram for the separation of desloratadine (5.4 min) and loratadine (7.4 min).

3.2. Selectivity

A mixed standard solution containing desloratadine and loratadine was determined under the proposed chromatographic conditions. The chromatogram is shown in Fig. 2, indicating the satisfactory resolution between the two drugs. Actually, the developed LC method was successfully used for the limit test of loratadine as an impurity in desloratadine drug substance. In this study, a mother liquor in the final step of synthetic process was also analyzed using the developed LC method and the chromatogram is given in Fig. 3, showing good resolutions and peak shapes of both desloratadine and its synthetic impurities.

For the further evaluation of the selectivity of the LC method, the forcedly degraded tablet sample solutions prepared by subjecting the tablet samples to such stress con-

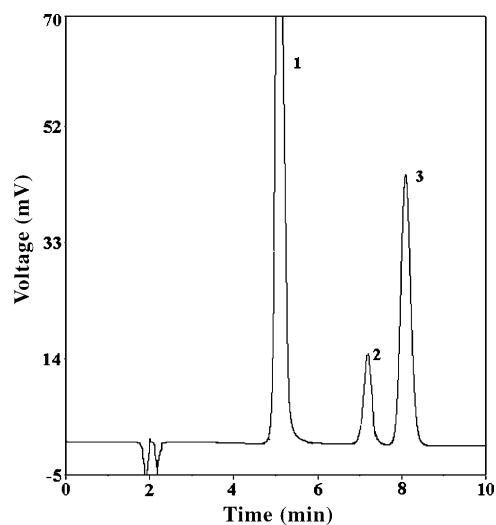


Fig. 3. LC chromatogram for the separation of desloratadine (5.4 min) and impurities (7.4 and 8.2 min) in the mother liquor of the synthetic process.

ditions as heat, light, acid and base were determined under the proposed chromatographic conditions. The obtained LC chromatograms for the separation of desloratadine from its degraded products in forcedly degradation tablet samples are shown in Fig. 4. As shown in Fig. 4, desloratadine exhibits a symmetric peak shape with a retention time at about 5.4 min and can be well resolved from the degradation products and the run time for one analysis is less than 10 min, which are favorable to the routine quality control of the product. The tablet excipients was also determined and found no interferences from the tablet excipients. The above results show that the developed LC method is selective for the determination of desloratadine in drug substance and pharmaceutical preparations.

3.3. Linearity

The linearity of the method was determined at five concentration levels ranging from 5.0 to 50.0 $\mu\text{g/ml}$ for desloratadine in triplicate. The calibration curve was constructed by plotting mean area response (A) against concentration (C) of the drug. The equation for calibration curve was $A = -1245.4 + 639.6 C$ ($r = 0.9997$). The results show that an excellent correlation exists between peak area and concentration of the drug within the concentration range indicated above.

3.4. Limit of quantitation

The limit of quantitation (LOQ) of desloratadine was experimentally verified by six injections at its LOQ concentration. The LOQ of desloratadine was found to be 0.10 $\mu\text{g/ml}$.

3.5. Precision

The system precision is determined by performing five replicate analyses of the same working solution and evaluated by relative standard deviation (R.S.D.) of the peak area of the analyte. The obtained R.S.D. value for desloratadine was 0.4%.

The method precision of the developed LC method was determined by preparing the tablet samples of the same batch in nine replicate determinations. The R.S.D. value of the assay results, expressed as a percentage of the label claim, was used to evaluate the method precision. The obtained R.S.D. value was 0.6% for the determination of desloratadine in tablets. The results for the system precision and method precision indicate the good precision of the developed method.

3.6. Accuracy

The accuracy of the developed method was evaluated by applying the developed method to synthetic mixtures of excipients to which known amounts of the drug corresponding to 80, 100 and 120% of label claim had been added. The accuracy was then calculated as the percentage of the

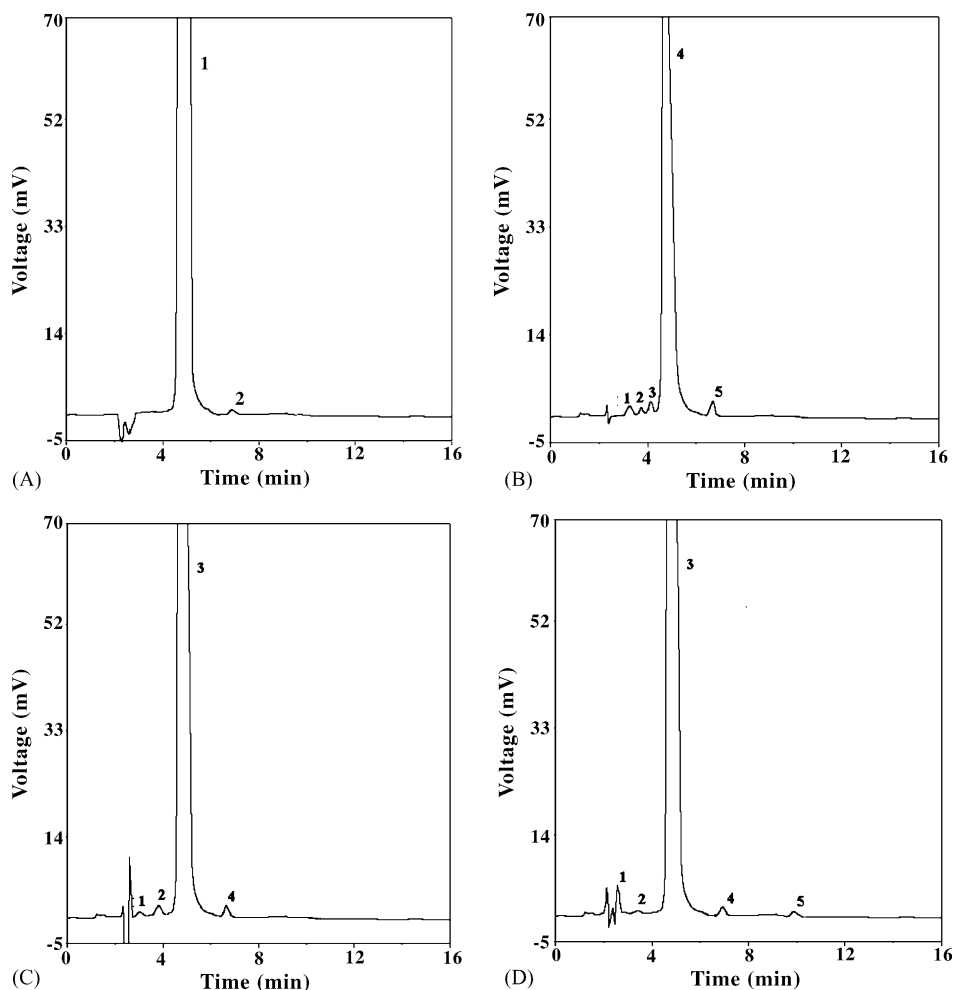


Fig. 4. Representative chromatograms for the separation of desloratadine from its degraded products in forcedly degradation tablet samples: (A) photodegradation; (B) thermal degradation; (C) acid degradation; (D) base degradation.

drug recovered from the formulation matrix. Mean recovery (Mean \pm S.D.) for desloratadine from the formulation is $99.6 \pm 0.7\%$ ($n=9$), indicating the good accuracy of the developed method for the determination of desloratadine in the drug product.

3.7. Solution stability

In order to demonstrate the stability of both standard and tablet sample solutions during analysis, both solutions were analyzed over a period of 5 h at room temperature. The results show that for both solutions, the retention time and peak area of desloratadine remained almost unchanged (R.S.D. % less than 2.0) and no significant degradation was observed within the indicated period, indicating that both solutions were stable for at least 5 h, which was sufficient for the whole analytical process.

3.8. Method application

The validated LC method was successfully applied for the assay of desloratadine in drug substance and tablet formu-

lation from three batches. Assay results for three batches of desloratadine tablets, expressed as the percentage of the label claim, were found to be 98.7, 100.6 and 98.9% ($n=3$), respectively, showing that the content of desloratadine in the tablet formulation conformed to the content requirements (90–110% of the label claim). The above results demonstrate that the developed LC method achieved rapid and accurate determination of desloratadine and can be used for the determination of desloratadine in drug substance and pharmaceutical formulations.

4. Conclusions

The developed LC method is simple and selective for simultaneous determination of desloratadine and loratadine possibly present in desloratadine drug substance and pharmaceutical formulations. It can be used for the process control of desloratadine synthesis and for the determination of desloratadine in drug substance and formulated products in ordinary laboratories.

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