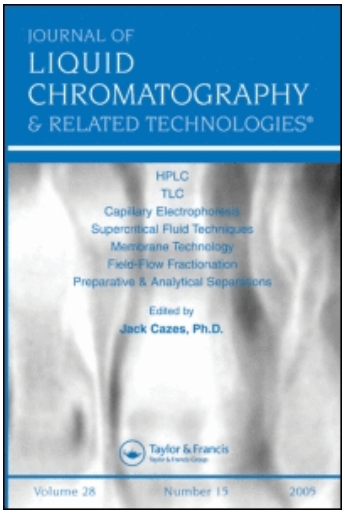

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Measurement of Ceftazidime Arginine in Aqueous Solution by HPLC

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MEASUREMENT OF CEFTAZIDIME ARGININE IN AQUEOUS SOLUTION BY HPLC

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ABSTRACT

Ceftazidime is used widely for the treatment of infections caused by gram-negative microorganisms. Ceftazidime arginine is its newest formulation available in the U.S.. It is reconstituted and stored in plastic syringes. A high-performance liquid chromatographic (HPLC) method was developed to measure ceftazidime arginine in aqueous solution to determine its stability during storage in plastic syringes. The chromatographic separation was achieved using an ultrasphere ODS column and mobile phase containing 89% 0.01M ammonium acetate buffer and 11% methanol, at a detection wave length of 254 nm. The retention time of ceftazidime arginine was about 4.27 minutes. The accuracy ranged from 98.6 to 99.8% and the coefficient of variation was less than 1%. The technique was used to determine the stability of ceftazidime arginine in sterile water for injection during storage for 24 hours in plastic syringes.

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INTRODUCTION

Ceftazidime is a parenteral third-generation cephalosporin. It is widely used for the treatment of infections caused gram-negative bacteria in seriously ill patients.[1] There are three FDA approved formulations of ceftazidime available as powders, which must be reconstituted prior to use in patients.

Ceftazidime arginine is the newest commercially available formulation, which produces less gas and fewer bubbles after reconstitution than two older sodium carbonate formulations of ceftazidime.[2] This offers an ease in its reconstitution in vials, and storage in plastic syringes prior to administration to patient . Plastic syringes are commonly used for drug storage and administration by syringe pumps. It is important to note, however, that no HPLC methods are available to measure ceftazidime arginine in aqueous solution to document its stability after reconstitution and storage in plastic syringes.

The purpose of this article is to describe a simple, rapid, accurate and reproducible HPLC method for the determination of ceftazidime arginine in an aqueous solution. The method was successfully used to determine the stability of ceftazidime arginine during storage in plastic syringes.

MATERIALS AND METHODS

Equipment

High performance liquid chromatography instrumentation included Hewlett Packard 1050 Series pump, autosampler, variable wave length detector, and an integrator (HP 3396A). Other equipments were a Beckman Ultrasphere ODS column (5μ, 4.6 x 250 mm) and a digital pH meter (Orion, model 701A).

Chemicals and Reagents

The chemicals and reagents included ammonium acetate (Aldrich, lot no. 03003KX), glacial acetic acid (Mallinckrodt, lot no. 2504 KAPM-A), methanol (Burdick & Jackson, lot no. BA 469), sulfuric acid (Fisher, lot no 746109), sodium hydroxide (Mallinckrodt, lot no. 7708KCAY), ceftazidime pentahydrate (Glaxo, lot no. AWS 27C), L-arginine (Glaxo, lot no. AWS 323), ceftazidime injectable formulation (Glaxo, lot no. A771/120), buffer solution, pH 7.00 (Fisher, lot no. 91090-24), buffer solution, pH 4.00 (Fisher, lot no. 910043-24), Sterile Water for Injection USP (Abbott, lot no. 46-506-DK).

Mobile Phase

The Mobile Phase was prepared with 89% 0.01 M ammonium acetate buffer and 11% methanol filtered through a 0.45μ nylon 66 filter, and then degassed with helium.

Sample Preparation

The Ceftazidime formulation was mixed with 10 mL sterile water for injection and drawn into five 20-mL plastic syringes (Becton-Dickinson, lot no. 10215). These syringes were stored for 24 hours at room temperature, and samples were drawn at 0 and 24 hours. The samples were then diluted 1:10 with mobile phase placed in amber sample vials and analyzed.

Standards Preparation

A stock solution was prepared with sterile water and diluted to yield concentrations of standards: 150, 125, 100, 75, and 50 mg/mL. The standards were then diluted in the same manner as the samples and analyzed.

Chromatographic Conditions

The flow rate was 1.5 mL/min. The detector was set at a wavelength of 254 nm and the injection volume was 10 μL. All measurements were performed at ambient temperature.

Stability-indicating method

In order to establish the stability-indicating nature of the method, ceftazidime arginine was subjected to forced base hydrolysis. Ceftazidime arginine was diluted 1:1 with 1.0 M sodium hydroxide and incubated for one hour at 60°C. The sample was then processed as described earlier to show that the quantitation of ceftazidime was not influenced by degradation products.

RESULTS AND DISCUSSION

Each chromatographic run required about 6 minutes. Ceftazidime eluted at about 4.27 minutes. Typical chromatograms of blank aqueous solution, and solution containing ceftazidime are shown in Figure 1 (A and B).

Linearity was determined by linear regression analysis of the data (Table 1). The correlation coefficient (r) was greater than 0.999. The accuracy of the method ranged from 98.6 to 99.8%; and the coefficient of variation was less than 1% (Table 2). Forced degradation by base hydrolysis did not affect the quantitation of ceftazidime (Figure 1, C).

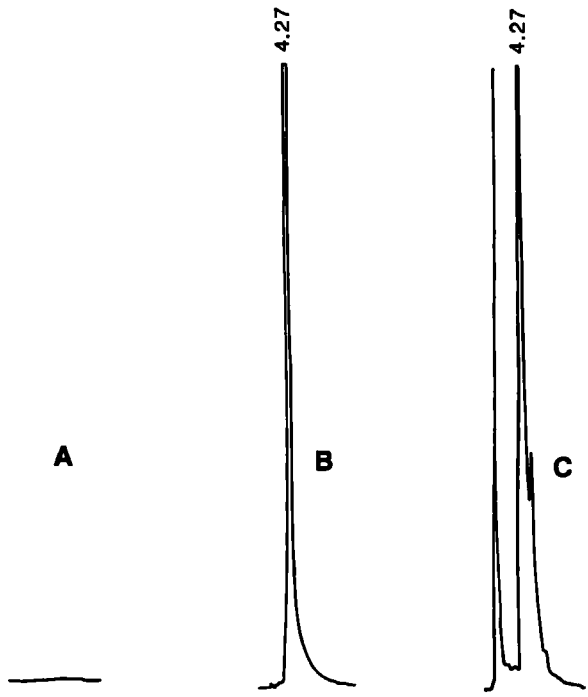

Figure 1. Chromatograms of blank aqueous solution (A), ceftazidime arginine (B), and ceftazidime after base hydrolysis (C).

Table 1. Peak heights of ceftazidime arginine at various concentrations.

Ceftazidime concentration mg/ mL	Peak height
50.0	2049321
75.0	3095181
100.0	4112913
125.0	5128466
150.0	6193740
Correlation coefficient	0.9999

Table 2. Accuracy of ceftazidime measurement.

Known concentration mg/mL	Concentration found (mean + SD) mg/mL	Percent of known conc. found
50.0	49.3±0.47	98.6
75.0	74.6±0.03	99.5
100.0	99.3±0.44	99.3
125.0	123.9±0.99	99.1
150.0	149.7±0.17	99.8

This method was used to determine the stability of ceftazidime arginine in an aqueous solution after reconstitution and storage for 24 hours in plastic syringes. Ceftazidime arginine remained stable as shown by its concentration exceeding 90% of the initial concentration during storage. Thus, it can be reconstituted and stored in plastic syringes for 24 hours prior to administration into patients.

The HPLC method described here has proved to be simple, rapid, accurate, and reproducible for the measurement of ceftazidime arginine in an aqueous solution. Further, it has been used to determine the stability of ceftazidime arginine in plastic syringes.

Acknowledgements

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