DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 16(8), 1435-1440 (1990)

QUANTITATION OF CEFADROXIL IN PHARMACEUTICAL DOSAGE FORMS USING HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY

Jagdish Parasrampuria and V. Das Gupta
Department of Pharmaceutics, University of Houston
1441 Moursund St., Houston, TX 77030

ABSTRACT

A high-performance liquid chromatography method for the quantitation of cefadroxil has been developed. The method has been applied to quantify cefadroxil in pharmaceutical dosage forms (capsules, suspensions and tablets) of 2 different manufacturers. A simple extraction procedure to extract cefadroxil from the dosage forms has been developed. The results were excellent with percent relative standard deviation of 1.2 based on 5 readings. A variety of inactive ingredients present in the dosage forms did not interfere with the assay procedure. After formulating, the suspensions were stable for longer periods at 5° than recommended on the label.

INTRODUCTION

Cefadroxil is a semisynthetic cephalosporine antibiotic intended for oral administration. It is widely used in the form of capsules, suspension and tablets. Degradation kinetics of cefadroxil in aqueous solutions have been reported (1). For these studies a stability indicating HPLC method was developed for the separation of decompostion products from the intact drug. The USP-NF method (2) for the quanti-

tation of cefadroxil in pharmaceutical dosage forms is based on its reaction with hydroxylamine.

The purposes of these investigations were to quantify cefadroxil in capsules, suspensions and tablets using the stability indicating HPLC method (1) after developing an internal standard and to determine the stability of suspensions after formulating and storage at 5°.

METHODOLOGY

Chemicals and Reagents: All the chemicals and reagents were USP-NF or ACS quality and used without further purification. The cefadroxil powder was supplied by Bristol Laboratories. All the dosage forms were of the commercial lots.

Apparatus: A high-pressure liquid chromatograph (Waters ALC 202) equipped with an injector (Rheodyne Model 7125), a multiple wavelength detector (Schoeffel's SF 770) and a recorder (Omniscribe 5213-12, Houston Instruments) was used. A C_{18} column (Microbondapak by Waters, 30 cm x 3.9 mm i.d) was the stationary phase.

Chromatographic Conditions: The mobile phase contained 2% by volume of acetonitrile in 0.01M aqueous buffer solution of ammonium acetate. The flow rate was 2.0 ml/min, the sensitivity was 0.04 AUFS (at 254 nm), the chart speed was 30.5 cm/hr and the temperature was ambient.

Preparation of Solutions: The stock solutions of cefadroxil and ceftazidime (the internal standard) in water (200 µg/ml each) were prepared fresh daily. The working standard was prepared by mixing 3.0 ml of the stock solution of cefadroxil with 6.0 ml of the stock solution of ceftazidime. Other dilutions were prepared as needed.

Extraction Procedure From The Capsules and Tablets: The powder from ten capsules was accurately weighed and ground to a fine powder. Ten

tablets were accurately weighed and then ground to a fine powder. A quantity of the powder representing 20.0 mg of cefadroxil was accurately weighed and occasionally stirred with 80 ml of water for 3-4 minutes. The mixture was brought to volume (100 ml) in a volumetric flask, shaken, filtered (Fisher's 9-803-5E filter paper), first 20 ml of the filtrate rejected and then collected for further dilution. A 3.0 ml quantity of the clear filtrate was mixed with 6.0 ml of the stock solution of ceftazidime (the internal standard).

Extraction Procedure from Suspension: The suspensions were formulated according to the directions on the label. A quantity of the suspension containing 50.0 mg of cefadroxil was diluted to 250 ml with water using a volumetric flask. The mixture was filtered as given above and 3.0 ml of the clear filtrate was mixed with 6.0 ml of the stock solution of the internal standard. After the initial assays, the suspensions were stored in the refrigerator (in the original bottles) and reassayed at the appropriate intervals.

Assay Procedure: A 20.0 µl quantity of the assay solution was injected into the chromatograph using the conditions described. For comparison, an identical quantity of the standard solution was injected after the assay sample eluted. The standard solution contained identical concentrations of the drug (based on the label claim) and the internal standard.

Calculations: Preliminary investigations indicated that the ratio of the peak heights (drug/internal standard) were directly related to the concentrations of the drug (range tested ± 30% of the standard concentration). Therefore, the results were calculated using a simple equation:

$$\frac{(R_{ph})_a}{(R_{ph})_s} \times 100 = \text{percent of the label claim found}$$

TABLE 1

ASSAY RESULTS OF THE DOSAGE FORMS AND SYNTHETIC MIXTURES

Dosage Form	Concentration mg/Cap or Tab or ml	Manufacturer	Percent of the Label Claim Found
Cefadroxil capsules	500	Mead Johnson	99.3
Cefadroxil capsules	500	Bristol-Myers	98.9
Cefadroxil tablets	1000	Mead Johnson	98.1
Cefadroxil tablets	1000	Bristol-Myers	99.1
Cefadroxil suspension	25	Mead Johnson	100.8
Cefadroxil suspension	25	Mead Johnson (different lot)	98.6
Cefadroxil suspension	50	Mead Johnson	100.8
Cefadroxil suspension	50	Bristol-Myers	102.1
Synthetic mixture 1	20 mg drug + 50 mg lactose		99.7
Synthetic mixture 2	20 mg drug + 50 mg dextrose		99.6

where $(R_{ph})_a$ is the ratio of the peak heights of the assay solution and $(R_{ph})_s$ that of the standard solution.

RESULTS AND DISCUSSION

The results indicate (Table 1) that all the dosage forms, capsules, suspensions and tablets can be assayed using the stability-indicating

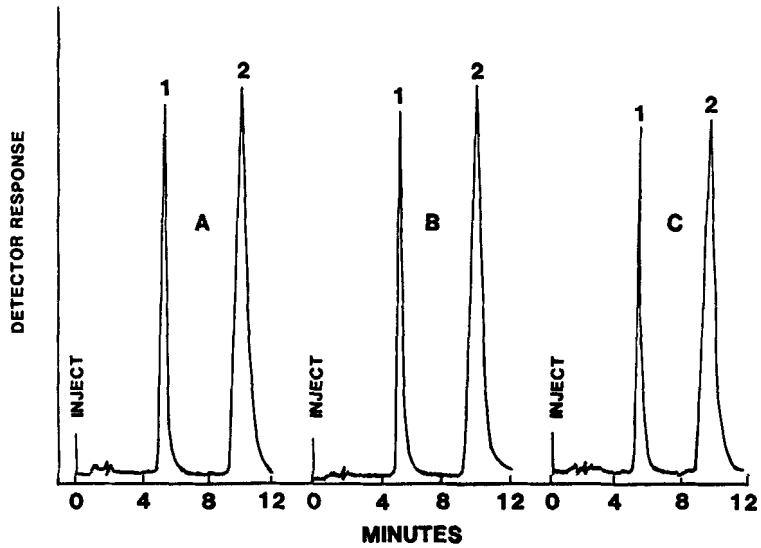

Figure 1 Sample chromatograms. Peak 1-2 are from cefadroxil and ceftazidime (the internal standrd), respectively. Chromatogram A is from the standard solution; B from capsules (Mead-Johnson); and C from suspension 1 in Table 1 (25 mg/ml, Mead Johnson). For chromatographic conditions, see text.

HPLC assay method (1). The separation of the drug from the internal standard developed was complete (Figure 1). The method is accurate and precise with a percent relative standard deviation based on 5 readings of 1.2.

The extraction procedure is very simple and a number of inactive ingredients, microcrystalline cellulose, magnesium stearate, D&E red #28, FD&C blue #1, FD&C red #40, gelatin, titanium oxide, FD&C yellow #6, flavors, polysorbate 80, sucrose, xanthan gum, tragacanth gum and the preservative sodium benzoate did not interfere with the assay pro-

cedure. The recovery from the synthetic mixtures was quantitative (Table 1).

The 15 and 42 day results of the formulated suspensions indicated that they were stable for longer period at 5° than recommended on the label (14 days). The results of 3 samples after 42 day storage at 5° were within 2-3% of the initial and no new peaks were found in the chromatograms.

After 42 day storage at 5° the suspensions were stored for 15 days at 25° (± 1°). The results indicated that two 50 mg/ml suspensions did not decompose more than 2% in 15 days at room temperature. However, both suspensions containing 25 mg/ml of cefadroxil decomposed by 5-6% in 15 days at 25°. No new peaks were found in the chromatograms even after storage at room temperature. It may not be necessary to store the constituted suspension in the refrigerator. After a total of 57 day storage, the maximum loss in potency of cefadroxil was 8.4%.

REFERENCES

1. A. Tsuji, E. Narashima and Y. Deguchi et al., J. Pharm. Sci., 70(10) 1120 (1981).
2. The United States Pharmacopeia, 21st Rev. The National Formulary, 16th Rev., The United States Pharmacopeial Convention, Rockville, MD, 1985 p. 171.