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Short Communication

Reversed-phase high-performance liquid chromatographic analysis of terfenadine

HANAN N. ALKAYSI,[1]* MUTAZ SHEIKH SALEM[1] and ADNAN A. BADWAN[2]

[1] *College of Pharmacy, Jordan University of Science and Technology, Irbid, Jordan*
[2] *The Jordanian Pharmaceutical Manufacturing Co., Naor, Jordan*

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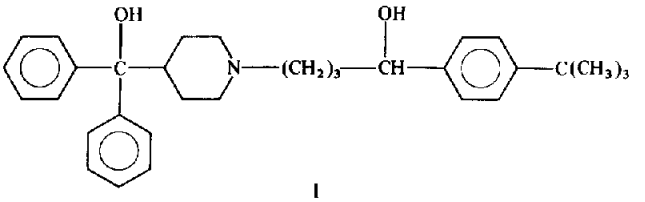
Introduction

Terfenadine (I) is a new non-sedating antihistamine. Clinically it is effective in the treatment of allergic conditions, but devoid of central nervous system depression and anticholinergic effects. The pharmacological aspects of terfenadine activity have been reviewed recently by Sorkin [1] and Carter [2]. Analytical methods used for the determination of terfenadine include radioimmunoassay and high-performance liquid chromatography [3, 4]. A study of the stability of terfenadine was reported recently [5].

This report details a reversed-phase high-performance liquid chromatographic method for the quantitative determination of terfenadine in bulk material and in dosage forms.



I

Experimental

Materials

Terfenadine powder was provided by the Jordanian Pharmaceutical Manufacturing Co., Jordan. Terfenadine tablets (60 mg) manufactured by Merrel Dow Pharmaceuticals Inc., USA (Teldane®) were purchased locally. Capsules (60 mg) and suspension (30 mg/5 ml) were donated by Jordanian Pharmaceutical Manufacturing Co. (Fenadine®).

* To whom correspondence should be addressed.

Ephedrine HCl was obtained from Sigma Chemical Co. (St Louis, MO, USA) additives and diluents were provided by Jordanian Pharmaceutical Manufacturing Co., acetonitrile and methanol were HPLC grade (J. T. Baker, Phillipsberg, NJ, USA). Other reagents were analytical grade available from BDH Chemical Co. (Poole, UK).

Instrument and Chromatographic Conditions

The analysis was carried out on a Beckman HPLC system consisting of a model 114A pump, an injection valve fitted with a 10 μl loop, a variable wavelength detector model 165 and a Spectra Physics model 4270 integrator. The column used was Altex Ultraspher C_{18} (25 cm × 4.6 mm i.d., particle size 5 μm). The mobile phase consisting of 0.1 M triethylammonium acetate buffer (pH 5.0)–acetonitrile–methanol (6.25:6.25:87.5, v/v/v) was used at a flow rate of 2 ml/min. The detection wavelength was 254 nm.

Standard curve

A reference sample of terfenadine was prepared by repeated crystallization from aqueous methanol and the purity was checked by HPLC, TLC and melting point. A standard curve was constructed over the concentration range 0.1–0.8 mg/ml using ephedrine hydrochloride as internal standard. The ratio of peak areas was plotted against concentration. Terfenadine concentrations in assay solutions were determined with reference to the calibration curve. The percentage recovery was determined by measurement of the amount of the drug in the examined dosage form, dividing by the weight claimed to be present by the supplier and multiplying by 100.

Sample preparation

The equivalent of 60 mg of terfenadine was weighed out, as representative of the contents of 20 units (tablets or capsules), suspended in 50 ml of methanol and sonicated for 10 min. A volume of 5 ml of this solution was withdrawn through a 0.45 μ membrane filter and diluted to 10 ml with methanol after the addition of 1 ml of internal standard solution (1.5 mg/ml of ephedrine HCl in methanol).

Sample preparation from suspension required raising the pH of the sample to 10 with sodium hydroxide solution. One millilitre of the sample (6 mg/ml) was diluted with methanol after the addition of internal standard.

Spiking with known amounts was carried out using a powder sample representing the average weight of a tablet or a capsule. Samples were analysed as described in the previous section.

Terfenadine adsorption study

The pH of 5-ml volumes of terfenadine solution (3 mg/ml) in methanol was adjusted with acetic acid or sodium hydroxide solutions. The methanolic solution was magnetically stirred with 500 mg of magnesium aluminum silicate (Veegum) for 10 min, 2 ml of the solution withdrawn through a 0.45 μ membrane filter and diluted to 10 ml for analysis. The same procedure was carried out using 50 mg of Veegum. A control solution was analysed simultaneously.

Results and Discussion

Few analytical methods have been reported for the determination of terfenadine that are applicable to dosage forms [3–5]. In this report, an analytical method suitable for

quality control purposes based on reversed-phase HPLC is described. A mobile phase consisting of methanol, acetonitrile and triethylammonium acetate buffer at an optimum pH of 5.0 is used. Ephedrine HCl, eluting after 3.4 min, proved to be an appropriate internal standard for the analysis. Since terfenadine required 4.2 min for elution the analysis may be completed within 5 min (Fig. 1).

The ready availability of the internal standard and the short analysis time afford advantages over the previously reported HPLC method [4] where the elution time of terfenadine was reported to be 14.5 min.

Linearity was established over the concentration range 0.1–0.8 mg/ml, with a correlation coefficient of 0.9999. The method enables the precise assay of terfenadine in bulk material as illustrated by the data in Table 1. Additives such as lactose, calcium dihydrogen phosphate, polyvinylpyrrolidone and microcrystalline cellulose commonly present in dosage forms do not interfere with the assay. However, when excess aluminum magnesium silicate (Veegum) is added, the recovery is not quantitative at lower pH values. The effect was studied further by analysing for possible adsorption of terfenadine on the surface of the suspension agent [6]. The detected concentration of the

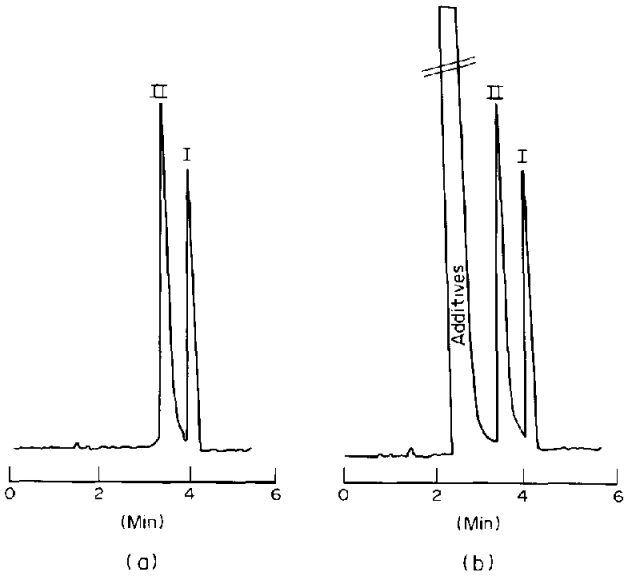


Figure 1
Chromatograms of terfenadine (I) and ephedrine HCl (II) in (a) tablets and (b) suspension.

Table 1
Percentage content of terfenadine in dosage forms and bulk material

	Mean	S.D. $n = 10$
Tablets	104.6	±0.68
Capsules	102.1	±0.85
Suspension	100.9	±0.83
Bulk material	100.7	±0.56

drug increased gradually with the increase in pH till complete and quantitative recovery was achieved at pH 10 and above (Fig. 2). Improved recovery from alkaline solutions suggests the possible adsorption of terfenadine cation onto the surface of the suspension [6].

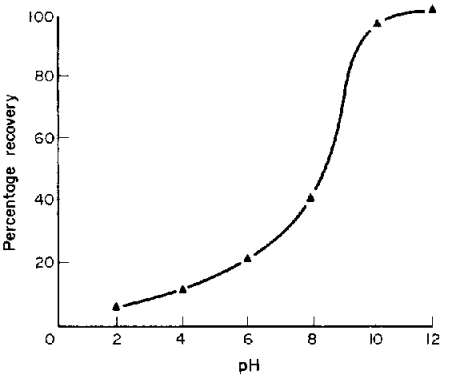


Figure 2
The effect of pH on the recovery of terfenadine from Veegum suspension.

Various dosage forms were analysed successfully. Typical chromatograms of terfenadine and internal standard in solid and liquid preparations are shown in Fig. 1a, b. Quantitative recovery from suspension samples required adjustment to pH 10 prior to analysis.

The reproducibility of the assay was tested by analysing samples representing the average weight of the single unit of the solid dosage form with a constant volume of the suspension. The results are listed in Table 1. Recovery from tablets, capsules and suspension spiked with known amounts of terfenadine was determined. The results are summarised in Table 2. The precision of the analytical procedure was expressed by the values of the relative standard deviation, which did not exceed 0.47 throughout the analysis.

Table 2
Percentage recovery from dosage forms spiked with known amounts of terfenadine

Amount added (mg)	% Recovery		
	Tablets	Capsules	Suspension
10	104.4 ± 0.45	101.2 ± 0.37	100.4 ± 0.41
20	104.5 ± 0.46	101.5 ± 0.47	101.1 ± 0.16
60	104.6 ± 0.25	100.6 ± 0.41	100.4 ± 0.47
80	103.6 ± 1.33	100.9 ± 0.25	100.5 ± 0.46
			$n = 5$

In conclusion, the reported reversed-phase HPLC analysis is shown to provide a facile and precise method for the quantitative determination of terfenadine in liquid and solid dosage forms.

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