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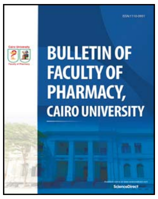

Original Article

TLC-densitometric and first derivative spectrophotometric methods for determination of cefoxitin-sodium in presence of its alkali-induced degradation product

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ABSTRACT

Two simple and accurate methods were developed for quantitative estimation of cefoxitin sodium in presence of its open ring alkali-induced degradation product. The first method was based on TLC separation of the drug from its alkali-induced degradation product followed by densitometric measurement of the intact drug at 254 nm. The proposed method obeys Beer's law in range (1–20 µg/band). The second method was first derivative (^{1}D) spectrophotometric method; was based on measurement of amplitude of first order spectra of cefoxitin sodium (in the range of 4–36 µg mL^{-1}) at 282 nm which showed zero crossing point of its degradation product. The two methods were validated according to ICH guideline for accuracy, precision and were successfully applied for the determination of the drug in pure form and pharmaceutical preparation in presence of its alkali-induced degradation product.

1. Introduction

Cefoxitin sodium is a semisynthetic cephamycin antibiotics, chemically named sodium 3-carbamoyloxymethyl-7-alpha-methoxy-7-[2-(2-thienyl)acetamido]-3-cephem-4-carboxylate[1] Fig. 1 and it was classified as a second generation cephalosporin. The most novel of chemical feature of cefoxitin sodium is the possession of an alpha-oriented methoxyl group in place of the normal H atom at C-7, as a result the steric bulk increased and a significant stability against β-lactamases obtained [2]. Cefoxitin sodium was produced by *Streptomyces lactamdurans* and used for the treatment of infections caused by anaerobic and mixed aerobic anaerobic infections, such as lung abscess and pelvic inflammatory disease, it is not absorbed from gastrointestinal tract so it's given parenterally as the sodium salt [3,4]. Literature survey reveals that HPLC methods were developed for the determination of cefoxitin sodium in pharmaceutical preparations [5] and in biological fluids [6–9] or by TLC method [10], and by LC-MS/MS [11], a flow injection chemiluminescent method was also reported for its determination [12]. Colorimetric determinations of cefoxitin sodium in pharmaceutical formulations and in biological fluids were reported [13–15], first derivative estimation of cefoxitin sodium in binary mixture with cephalothin [16], second derivative estimation of cefoxitin sodium in presence of its acid-induced degradation products [17] and spectrofluorimetric analysis [18] were described for its determination.

In this paper, thin layer chromatography (TLC)-densitometric method and first derivative (^{1}D) spectrophotometric method were applied for determination of cefoxitin sodium in presence of its alkali-induced degradation product as they have considerable spectral overlapping.

2. Experimental

2.1. Instruments

2.1.1. Instrument for TLC-densitometric method

- Camag TLC scanner with WINCATS computer software (Switzerland).
- Precoated TLC-plates consisted of silica gel 60 F_{254} (20 cm × 20 cm, 0.25 mm), (Fluka chemie, Switzerland).
- Hamilton 25-µL microsyringe (Germany).
- UV lamp with short wavelength, 254 nm (Desega- Germany).
- Chromatographic tank (25 × 25 × 9 cm).
- Jenco digital pH/temp. meter with Jenway double junction glass

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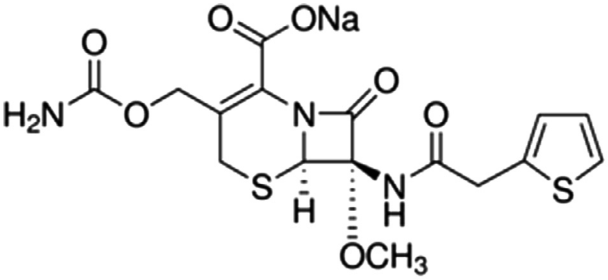

Fig. 1. Chemical structure of cefoxitin sodium.

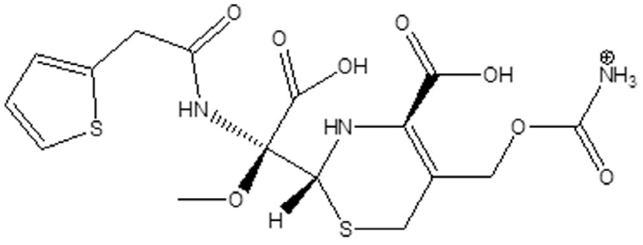

Fig. 2. Cefoxitin sodium alkali-induced degradation product.

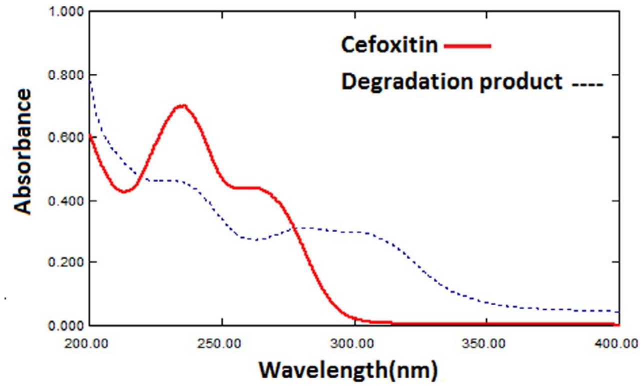

Fig. 3. Zero order absorption spectra (20 µg mL^{-1}) of cefoxitin sodium (———) and (20 µg mL^{-1}) of cefoxitin alkali-induced degradation product (········) using water as solvent.

electrode (UK).

2.1.2. Instrument for first derivative (^1D) spectrophotometric method

SHIMADZU dual beam UV–visible spectrophotometer (Kyoto/ Japan), model UV-1650 PC connected to IBM compatible and aHP1020 laser jet printer. The bundled software, UV-Probe personal spectroscopy software version 2.1 (SHIMADZU) was used. The spectral band was 2 nm and scanning speed is 2800 nm/min and 1 nm data interval

2.2. Chemicals and reagents

(a) Cefoxitin Sodium 98.8% was kindly supplied by Pharco B International Co., Cairo, Egypt. Lot No.12052036
(b) Primafoxin® 1 gm vial for IV injection & IV infusion, labeled to contain 1 gm of cefoxitin sodium per vial, Batch No. (109), the product of Pharco B international Co., Egypt, were purchased from local pharmacies
(c) 0.1 N Hydrochloric acid, 0.1 N Sodium hydroxide (El-Nasr Co., Egypt).
(d) Chloroform, methanol, acetonitrile, conc. ammonia, triethylamine, hexan (Sigma-Aldrich, USA).
(e) Distilled water used was freshly double distilled.

2.3. Standard solutions

2.3.1. Standard solution of intact cefoxitin sodium

Stock solution (2 mg mL^{-1}) was prepared by dissolving 200 mg of cefoxitin sodium in 80 mL methanol (in case of TLC-densitometric method) or in 80 mL water (in case of first derivative method), the volume was then completed to 100 mL with the same solvent for each method, methanolic solution and aqueous solution were stable at least for 3 days at room temperature. While aqueous solution was stable at least 15 days when stored at 5 °C in the dark [16].

2.3.2. Cefoxitin sodium alkali-induced degradation product stock solution [19,20]

Cefoxitin sodium alkali-induced degradation product stock solution (2 mg mL^{-1}) was prepared by transferring 200 mg of cefoxitin sodium to a 100-mL round bottomed flask containing 30 mL 0.1 N NaOH, then was refluxed for 10 min and cooled at room temperature, the resulting mixture was neutralized with 0.1 N HCl and then was evaporated to

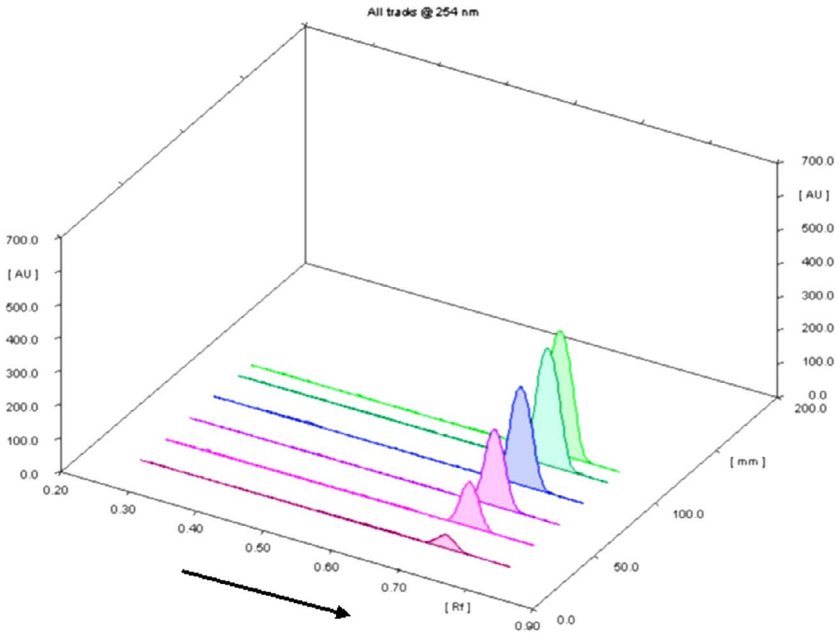

Fig. 4. (3D) Densitogram of cefoxitin sodium (1–20 µg/ band) at 254 nm using methanol as solvent.