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Stability indicating methods for the analysis of cefprozil in the presence of its alkaline induced degradation product

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ABSTRACT

Three simple, specific, accurate and precise spectrophotometric methods were developed for the determination of cefprozil (CZ) in the presence of its alkaline induced degradation product (DCZ). The first method was the bivariate method, while the two other multivariate methods were partial least squares (PLS) and spectral residual augmented classical least squares (SRACLS). The multivariate methods were applied with and without variable selection procedure (genetic algorithm GA). These methods were tested by analyzing laboratory prepared mixtures of the above drug with its alkaline induced degradation product and they were applied to its commercial pharmaceutical products.

1. Introduction

Cefprozil(6R,7R)-7-[(R)-2-Amino-2-(p-hydroxyphenyl)acetamido]-8-oxo-3-(1-propenyl)-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid monohydrate (Fig. 1) is bactericidal used in the treatment of susceptible infections including upper and lower respiratory tract, skin and soft tissue infections. It was classified as a second generation Cephalosporins, beta-lactam and other inhibitors of cell wall synthesis [1–3]. Literature survey reveals that spectrophotometric [4–15], HPLC [16–19], HPTLC [20] and flow injection chemiluminescent [21] methods were developed for the determination of cefprozil in pharmaceutical formulations and in biological fluids. In this paper, three different spectrophotometric methods were applied for the analysis of cefprozil in the presence of its alkaline induced degradation product, namely; bivariate spectrophotometric method [22–24], partial least squares (PLS) [25–28] and spectral residual augmented classical least squares (SRACLS) [29]. It is well known that increasing the number of informative variables included in building the model results in a more robust model. So bivariate and multivariate techniques should be more robust than univariate techniques. Moreover, a variable selection method namely genetic algorithm [30–33] was applied on PLS and SRACLS to obtain less complex models by elimination of uninformative variables.

2. Experimental

2.1. Instruments

SHIMADZU dual beam UV–visible spectrophotometer (Kyoto/Japan), model UV-1800 PC connected to IBM compatible and a HP1020 laser jet printer. The bundled software, UV-Probe personal spectroscopy software version 2.43 (SHIMADZU) was used. The spectral band was 2 nm and scanning speed is 2800 nm/min and 1 nm data interval.

2.2. Software

All chemometric methods were implemented in Matlab 8.2.0.701 (R2013b). PLS and SRACLS were performed with our own written

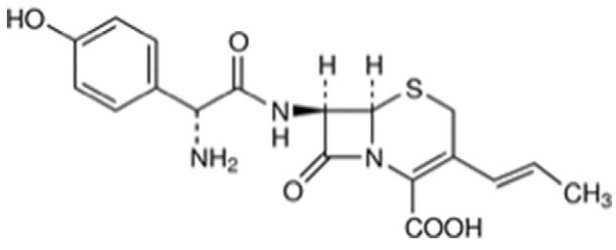

Fig. 1. Chemical structure of cefprozil.

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Table 1
The 5-level, 2-factor experimental design shown as concentrations of the mixture components in μg/mL.

Mix. no.	CZ	DCZ
1	20	20
2	20	16
3	16	16
4	16	24
5	24	18
6	18	24
7	24	20
8	20	18
9	18	18
10	18	22
11	22	24
12	24	22
13	22	20
14	20	24
15	24	24
16	24	16
17	16	22
18	22	16
19	16	20
20	20	22
21	22	22
22	22	18
23	18	16
24	16	18
25	18	20

The shaded rows represent the calibration set.

codes in Matlab. The *t*-test and *F*-test were performed using Microsoft Excel. One way ANOVA test was performed using GraphPad Prism version 5 (GraphPad, San Diego, CA).

2.3. Chemicals and reagents

(a) Cefprozil monohydrate certified to contain (99.30%) was kindly supplied by GlaxoSmithKline for pharmaceuticals, Cairo, Egypt.
(b) Pharmaceutical preparations: "Cefzil" tablets: (batch number 033762) containing 530 mg of cefprozil monohydrate per tablet.
(c) Solvent: distilled water.

2.4. Standard solutions for bivariate method

(a) Stock solution (0.5 mg/mL) was prepared by transferring 0.05 g of cefprozil monohydrate to 100 mL volumetric flask, dissolving in distilled water and the volume was then completed to the mark.
(b) Preparation of the alkaline degradation product (DCZ):

Stock solution was prepared by treating 0.05 g of cefprozil monohydrate with 10 mL 1 N NaOH and allow to stand for ten minutes at ambient temperature then neutralized with 1 N HCl and evaporated to dryness. The residue was dissolved in water, filtered into 100 mL measuring flask and completed to volume with the distilled water to obtain stock solution of alkaline induced degradation product derived from 0.5 mg/mL [14]. Aliquots of different concentrations of cefprozil degradation product (DCZ) were accurately transferred into series of 10 mL volumetric flasks and the volumes were completed to the mark with water. These solutions were scanned in range 200–400 nm and stored in the computer.

2.5. Standard solutions for chemometric methods

(a) Working solution (100 μg/mL) was prepared by transferring 0.01 g of cefprozil monohydrate to 100 mL volumetric flask, dissolving in distilled water and the volume was then completed to the mark.
(b) Preparation of the alkaline degradation product (DCZ):

Working solution was prepared by treating 0.01 g of cefprozil monohydrate with 10 mL 1 N NaOH and allow to stand for ten minutes at ambient temperature then neutralized with 1 N HCL and evaporated to dryness. The residue was dissolved in water, filtered into 100 mL measuring flask and completed to volume with the distilled water to obtain stock solution of alkaline induced degradation product derived from 0.1 mg/mL.

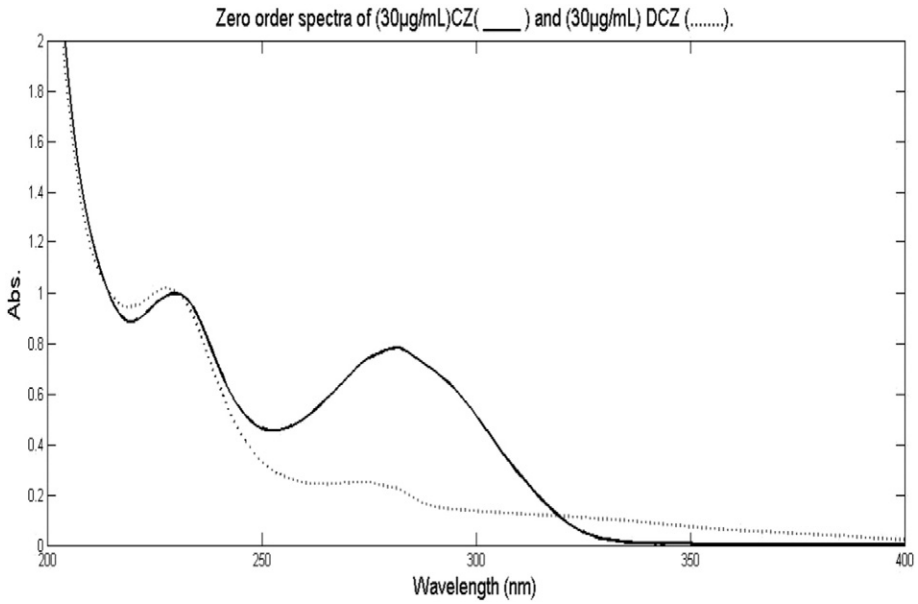

Fig. 2. Zero order spectra of (30 μg/mL) CZ (____) and (30 μg/mL) DCZ (.....).