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Research Article

Determination Of Ciprofloxacin With Zero-, First- And Second-Order Derivative Spectrophotometric Method In Water And Methanol Media

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ABSTRACT:
Ciprofloxacin is a synthetic fluoroquinolone derivative antibiotic used to treat various bacterial infections. Simple, fast and reliable zero-, first- and second-order derivative spectrophotometric methods were developed for determination of ciprofloxacin in two pharmaceutical dosage forms. The solutions of standard and the sample were prepared in methanol and water medium. The quantitative determination of the drug was carried out using the zero-, first- and second-order derivative values measured 270-310 nm (N=6) Calibration graphs constructed at their wavelengths of determination were linear in concentration range of ciprofloxacin using peak to zero 2.00-10.00 µm/mL for zero-, first- and second-order derivative spectrophotometric method. The developed methods were successfully applied for the assay of pharmaceutical dosage forms for two solvent media which do not require any preliminary separation or treatment of the samples. The details of statistical treatment of analytical data are also presented (p>0.05).

Keywords : Ciprofloxacin, derivative spectrophotometric method, different media

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1. INTRODUCTION

Ciprofloxacin has a chemical structure of 1-cyclopropyl-6-fluoro-1.4-dihydro-4-oxo-7-(with piperazine) quinolone-3-carboxylic acid (Fig.1.). It is a broad-spectrum antibacterial agent in the structure a fluoroquinolone having against gram positive and gram-negative bacteria. It shows its activity by appearing as bacterial DNA gyrase enzyme Thus bacteria are not resistant to fluoroquinolones through plasmid or R factor mediated mechanisms. and is not vulnerable to degradation by bacterial inactivating mechanisms. Ciprofloxacin is usually used in the infections of gastrointestinal tract, urinary tract, and skin tissues by bacteria [1-8].

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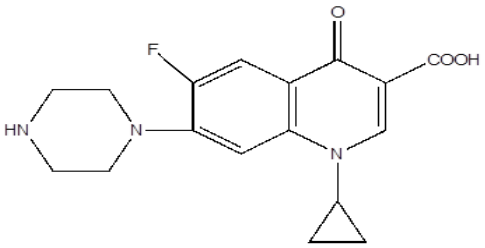

Figure 1. Chemical structure of ciprofloxacin

Various assay methods (HPLC, polarography, adsorptive stripping voltametry and titrimetry) have been reported for determination ciprofloxacin in biologic material and in pharmaceutical preparation [1,4,8-11]. Few spectrophotometric methods have been reported for determination of ciprofloxacin in pharmaceutical preparations. These included complex formation with eosin, paladyum and iron, through the formation of charge transfer complex with chlorinic acid [11-16].

Based on the above reported methods, it was thought necessary to developed simple, fast and accurate spectrophotometric method for determination of ciprofloxacin in pharmaceutical preparations. The aim of this work was to investigate the utility of zero-, first- and second-order derivative spectrophotometry in assay of ciprofloxacin in pharmaceutical preparations without the necessity of sample pre-treatment. In this study, zero-, first- and second-order derivative UV spectrophotometric methods are developed and validated for the determination of ciprofloxacin in two different solvent media (water and methanol). The developed methods were applied to two different commercial preparations as tablet and eye drop. The results obtained from zero-, first- and second-order derivative spectrophotometry to two different solvent media (water and methanol) were compared.

2. MATERIALS AND METHODS

2.1. Instrument

The spectrophotometric measurements were performed on a Thermospectronic double beam UV Vis spectrophotometer, using 1.0 cm quartz cells, connected to Lexmark lazier printer. The spectral bandwidth was 2 nm and wavelength scanning speed was 600 nm min-1. The derivative spectra of test and reference solutions both water and methanol were recorded over the range 270-310 nm with $\Delta\lambda$ = 21.0 nm.

2.2. Materials and Reagents

Reference ciprofloxacin was kindly supplied by the Bilim Drug Company in Turkey. It was tested for purity by controlling its melting point, UV and IR spectrum. The impurity was not found. Cipro tablets, containing 500 mg ciprofloxacin, and Sipragut eyedrop, containing 3.5 mg/mL ciprofloxacin, were obtained from local market in Erzurum-Turkey. All experiments were performed with analytical reagent grade purchased from Merck.

2.3. Standard Solutions of Ciprofloxacin

Stock solutions of ciprofloxacin were prepared at a concentration of 20 μg/mL both methanol and water medium. The solutions kept at room temperature and strict. Stability of ciprofloxacin stock solutions were tested during a period of two days and found to be stable. Working standard solutions were daily prepared by diluting stock solutions at the concentrations of 2, 4, 6, 8 and 10 μg/mL both methanol and water media. Water and methanol were used as blank solution.

2.4. Procedures

A total 5 tablets of ciprofloxacin accurately weighed and powdered. An amount of this powder corresponding to one tablet ciprofloxacin content was weighed and transferred in a 100 mL volumetric flask. 15 mL methanol was added and the flask was sonicated for 5 min. The flask was filled to volume with methanol and the same procedure was made for water. 1 mL of eye drop was transferred to 100 mL volumetric flask, 15 mL methanol was added and the flask was sonicated for 5 min. The flask was filled to volume with methanol and the same procedure was made for water

2.5. Method Validation

The validation of method was carried out by establishing specifity, linearity, recovery values, limits of detection (LOD), limit of quantification, within- and between-day precision and accuracy according to International Conference on Harmonization guidelines (ICH) [17,18] for validation of analytical procedures.

3. RESULTS AND DISCUSSION

3.1. Optimization of Conditions

The solvent, the degree of derivation, the wavelength ranges and N values were chosen in order to optimize the conditions. Optimum results were obtained in measuring wavelength range 270-310 nm, N=6 ($\Delta\lambda$ = 21.0 nm) for zero-, first- and second-order derivative spectrophotometry. UV spectrum of ciprofloxacin gives a single peak at 286 nm. The ^{1}D curve displayed a maximum at 283 and a minimum at 289 nm, while the ^{2}D curve showed a maximum at 280 nm and a minimum at 286 nm both water and methanol medium (Fig.2.). Zero-, first- and second-order derivative UV spectrum of Cipro tablets and Sipragut eyedrop solution both water and methanol medium are shown in Fig. 3 and 4, respectively.

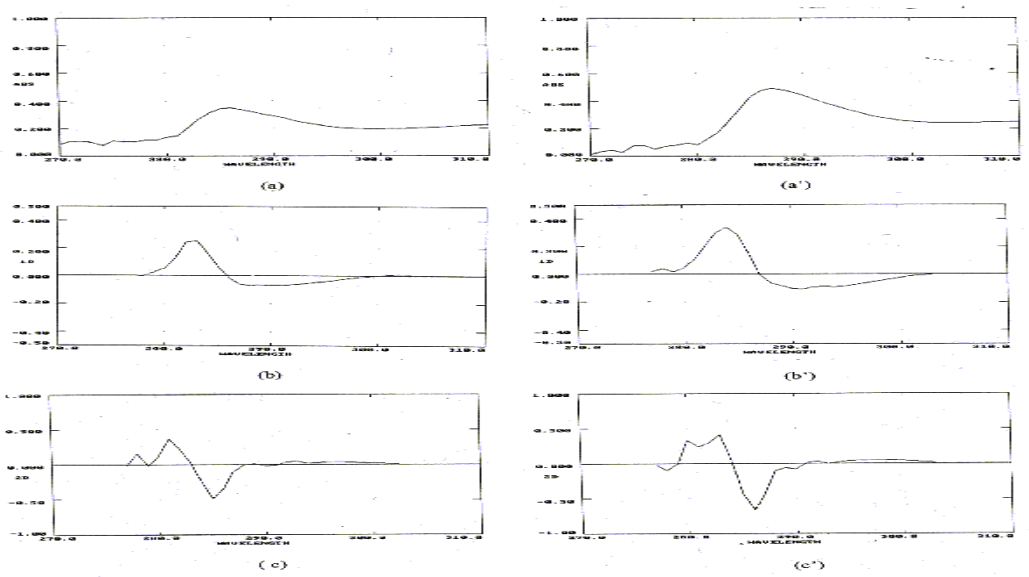

Figure 2. Zero-, First- and Secon-order derivative spectrum of standard ciprofloxacin solution (7µg/mL); in water medium (a,b,c) and in methanol medium (a′,b′,c′)

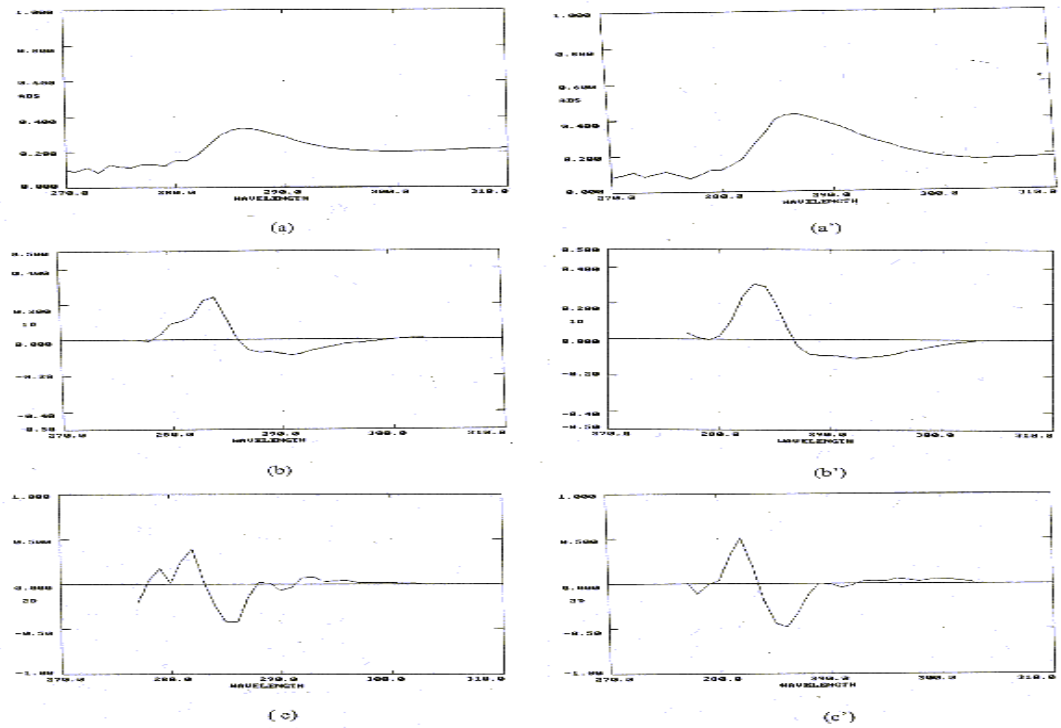

Figure 3. Zero-, First- and Secon-order derivative spectrum of Cipro 500 mg tablet solution (7µg/mL);in water medium (a,b,c) and in methanol medium (a′,b′,c′)

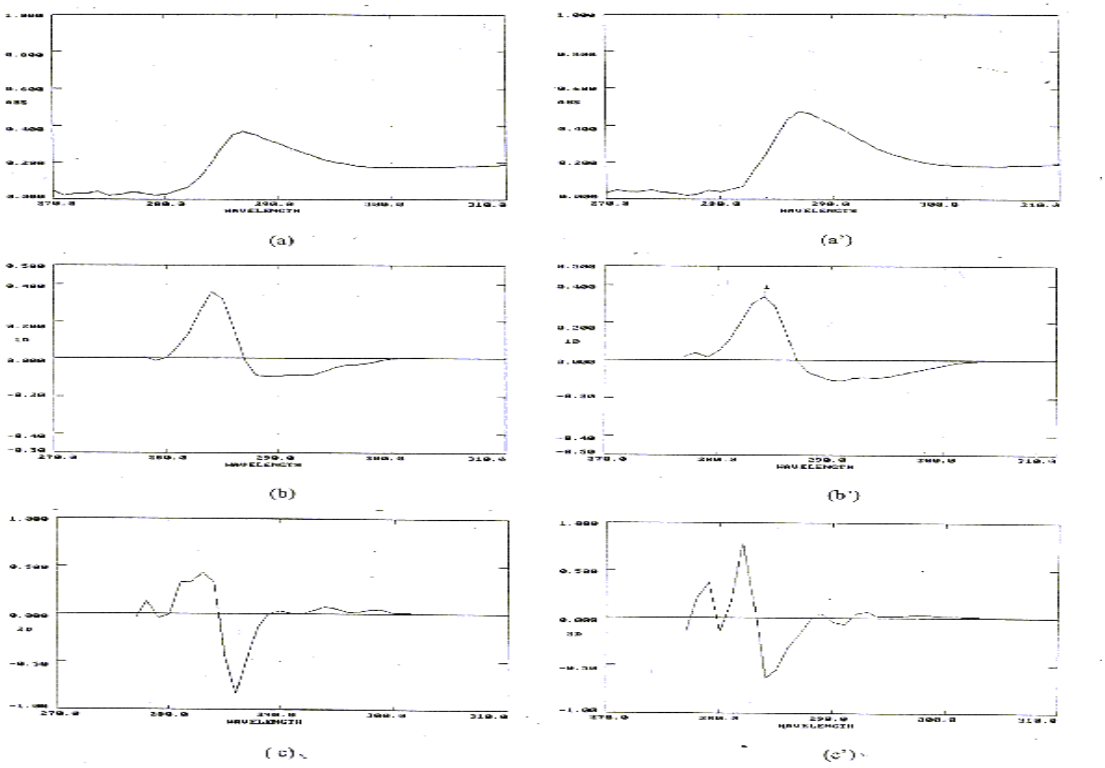

Figure 4. Zero-, First- and Secon-order derivative spectrum of commercial sterilize sipragut eyedrop solution (7µg/mL);in water medium (a,b,c) and in methanol medium (a′,b′,c′)

3.2. Linearity of Calibration Curves

In quantitative analysis, the standard calibration curves for zero-, first- and second-order derivative spectrophotometry of ciprofloxacin in methanol and water medium were constructed by plotting derivative absorbance versus concentration under the experimental conditions described and evaluated by using correlation coefficient. Regression analysis using the method of least-squares was made for the slope, intercept and correlation coefficient values (Table 1 and 2). The regression equations of calibration curves for methanol medium were y=0.0655x + 0.0289, y= 0.0266x + 0.0339 and y= 0.4450x + 0.1230 for zero- first and second-order derivative spectrophotometric methods, respectively. For water medium, the regression equations of calibration curves were y=0.0442x + 0.0271, y= 0.0354x + 0.0565 and y= 0.0805x + 0.0091 for zero-first and second-order derivative spectrophotometric methods, respectively. The linearity ranges were found to be 2-10 µg/mL for both methanol and water media.

The correlation coefficient of standard calibration curves for zero-, first- and second-order derivative spectrophotometry of ciprofloxacin in methanol medium were higher that of ciprofloxacin in water media. Thus it has been found that the methanol solution is better but the correlation coefficients obtained from all of calibration curves of each of these solutions were showed good linearity.

Table 1. Features of the calibration curves zero-first–second-order derivatives of ciprofloxacin in methanol

Features	Zero-order	First-order	Second-order
Regression equation	y=0.0655x +0.02892	y=0.0266x +0.0339	y=0.4450x + 0.1230
RSD%	0.52-4.53	0.58-5.12	0.63-6.48
Correlation coefficent (r)	0.9998	0.9972	0.9945
Linear range (µg/mL)	2-10	2-10	2-10

Table 2: Features of the calibration curves zero-first–second-order derivatives of ciprofloxacin in water

Features	Zero-order	First-order	Second-order
Regression equation	y=0.0442x +0.0271	y=0.0354x +.0565	y=0.0805x +0.0090
%RSD	0.60-5.37	0.65-6.24	0.71-7.25
Correlation coefficent (r)	0.9965	0.9874	0,9884
Linear range (µg/mL)	2-10	2-10	2-10

3.3. Sensitivity

In methanol medium, the limit of quantification (LOQ) for ciprofloxacin was found as 0.5 µg/mL, 0.65 µg/mL and 0.70 µg/mL and the limit of detection (LOD) was found as 0.1 µg/mL (s/n > 2), 0.35 µg/mL and 0.75 µg/mL for zero-, first- and second- order derivative spectrophotometry.

In water medium, the limit of quantification (LOQ) for ciprofloxacin was found as 0.6 µg/mL, 0.85 µg/mL and 0.89 µg/mL and the limit of detection (LOD) was found as 0.2 µg/mL (s/n > 2), 0.55 µg/mL and 0.95 µg/mL for zero-, first- and second-order derivative spectrophotometry. The determinations of different concentration levels were carried out for each drug to test sensitivity, quantitation and reproducibility and of zero-, first- and second- order derivatives values.

3.4. Repeatability

Repeatability is given as inter- and intra-day precision and accuracy where evaluated by analyzing three different concentrations and three different day of ciprofloxacin. The inter-day precision was evaluated by comparing the linear regressions of three standard plots prepared on three different days. Six replicate determinations at three different concentrations (the concentration range 3, 7 and 9 µg/mL for ciprofloxacin in methanol and water) were carried out to test the precision of this method. The experimental results obtained from zero-, first- and second-order derivative spectrum of ciprofloxacin both methanol and water are shown in Table 3, 4 and 5, respectively

The RSD values from ciprofloxacin in methanol and water media, respectively, were found to be 0.51-8,6% and 1.52- 9.5% for zero-order derivative, 1.27-5.72% and 3.21-8.48% for first-order derivative and 2.31-5.43% and 3.12-8.38% for second-order derivative spectrophotometry. These data indicated that the developed methods have a good repeatability.

Table 3. Summary of assay precision data for ciprofloxacin in methanol and water intra-day, inter day by UV-Vis spectrophotometry

		Intra day			Inter-day		
Sample	Concentration (µg/mL)	X	SD	RSD %	X	SD	RSD %
Ciprofloxacin (water)	3	0.1280	0.0550	4.30	0.1300	0,0083	6,41
	5	0.2280	0.0036	1.56	0.2310	0.0190	8.54
	7	0,3150	0.0048	1.52	0.3190	0.0300	9.50
Ciprofloxacin (methanol)	3	0.1940	0.0009	0.51	0.1820	0.0039	2.16
	5	0.3620	0.0054	1.49	0.3120	0.0270	8.60
	7	0,4430	0.0035	0.79	0.4170	0.0148	3.57

SD[a] : Standard deviation of six replicate determinations, RSD: % Relative standard deviation

Table 4. Summary of assay precision data for ciprofloxacin in methanol and water intra-day, inter day by first - order spectrophotometry

		Intra day			Inter-day		
Sample	Concentration (µg/mL)	X	SD	RSD %	X	SD	RSD %
Ciprofloxacin (water)	3	0.1100	0.0093	8.48	0.1190	0.0109	9.21
	5	0.1470	0.0066	4.49	0.1530	0.0049	3.21
	7	0.2250	0.0175	7.80	0.2380	0.0127	5.37
Ciprofloxacin (methanol)	3	0.1470	0.0053	3.65	0.1580	0.0020	1.27
	5	0.2370	0.0089	3.75	0.4510	0.0233	5.17
	7	0.3130	0.0139	4,44	0.2310	0.0132	5.72

SDa : Standard deviation of six replicate determinations, RSD: % Relative standard deviation

Table 5. Summary of assay precision data for ciprofloxacin in methanol and water intra-day, inter day by second-order spectrophotometry

		Intra day			Inter-day		
Sample	Concentration (µg/mL)	X	SD	RSD %	X	SD	RSD %
Ciprofloxacin (water)	3	0.2420	0.0147	6.09	0.2390	0.0074	3.12
	5	0.2930	0.0163	5.56	0.2870	0.0130	4.56
	7	0.4400	0.0368	8.38	0.4350	0.0322	7.42
Ciprofloxacin (methanol)	3	0.2600	0.0141	5.43	0.2710	0.0111	5.12
	5	0.6050	0.0250	4.14	0.7210	0.0166	2.31
	7	0.7990	0.0271	3.39	0.6100	0.0212	3.48

SD[a] : Standard deviation of six replicate determinations, RSD: % Relative standard deviation

4. CONCLUSIONS

An analytical zero-, first- and second-order derivative spectrophotometric methods was developed and validated thoroughly for quantitative determination of ciprofloxacin in two pharmaceutical formulations (tablet and eye drop) in both methanol and water media.

The present method was found to be simple, accurate and reproducible which can be directly and easily applied of the pharmaceutical formulations of Ciprofloxacin.

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