SIMULTANEOUS UV SPECTROPHOTOMETRIC METHODS FOR ESTIMATION OF CEFADROXIL AND PROBENECID IN TABLET DOSAGE FORM

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RESEARCH ARTICLE

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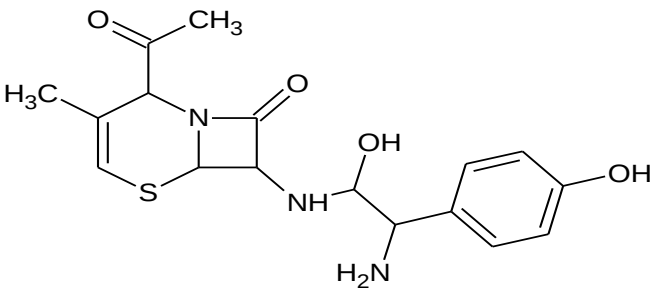
ABSTRACT:

Two methods for simultaneous estimation of Cefadroxil and Probenecid in combined tablet dosage form have been developed. The first UV spectrophotometric method was a determination using the simultaneous equation method at 233 nm and 247 nm. The second UV spectrophotometric method is the Q – analysis (absorption ratio) method, which involves the formation of absorbance equation at 242 nm (Isobestic point) and at 247 nm the maximum absorption of Probenecid . The linearity ranges for Cefadroxil and Probenecid both were 10-60µg/ml respectively. The accuracy of the methods was assessed by recovery studies was found to be 99.43±0.75 and 99.69±0.40 for simultaneous equation method and 99.23±0.34 and 99.56±0.16 for absorption ratio method for Cefadroxil and Probenecid respectively. These methods are simple, accurate and rapid; those require no preliminary separation and can therefore be used for routine analysis of both drugs in quality control laboratories.

Key words: Cefadroxil, Probenecid, Q–analysis spectrophotometric, Simultaneous equation method.

Introduction:

Cefadroxil chemically a 7-[[2-amino -2-(4-hydroxyphenyl) acetyl] amino]-3-methyl-8-oxo-5-thia-1-azabicyclo [4.2.0] oct-2-ene-2-carboxylic acid Cefadroxil.(1)

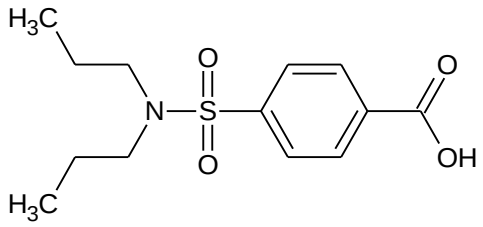


Chemical structure of Cefadroxil

Cefadroxil, a first-generation cephalosporin antibiotic, is used to treat urinary tract infections, skin and skin structure infections, pharyngitis and tonsillitis. Like all beta-lactam antibiotics, cefadroxil binds to specific penicillin-binding proteins (PBPs) located inside the bacterial cell wall, causing the inhibition of the third and last stage of bacterial cell wall synthesis. Cell lysis is then mediated by bacterial cell wall autolytic enzymes such as autolysins; it is possible that Cefadroxil interferes with an autolysin inhibitor. Literature survey revealed that Cefadroxil was qualitatively assayed in biological fluids either individually or in presence of other antibacterial drugs using liquid chromatography 5, other new methods and using Hydrotope are also there for the determination of Cefadroxil. (2 - 4)

Probenecid is a Uricosoric agent used in gout therapy. When Cefadroxil is co-administered with Probenecid, the renal excretion of Cefadroxil is inhibited. The combination is used in gastrointestinal tract and respiratory tract infections. The prototypical Uricosuric agent. It inhibits the renal excretion of organic anions and reduces tubular reabsorption of urate. Probenecid has also been used to treat patients with renal impairment, and, because it reduces the renal tubular excretion of other drugs, has been used as an adjunct to antibacterial therapy. (5) The mechanism by which Probenecid inhibits renal tubular transport is not known, but the drug may inhibit transport enzymes that require a source

of high energy phosphate bonds and/or non specifically interfere with substrate access to protein receptor sites on the kidney tubular.



Chemical structure of Probenecid

Materials and methods:

Pharmaceutically pure samples of CEF and PROB were obtained as gifts from Curex Pharmaceuticals Industries Ltd Jalgaon. Methanol was used as solvent in the study. Double beam UV/Vis spectrophotometer Shimadzu model 1800 with a pair of 10mm matched quartz cells was used to measure absorbance of the resulting solution.

Preparation of standard stock solution:

Accurately 10 mg each of CEF and PROB was weighed separately and transferred to two different 100ml volumetric flask .volume was made up to the mark with Methanol. The standard stock solutions (100µg/ml) were further diluted separately to obtain working standard of concentration 10µg/ml of CEF and PROB each.

Study of spectra and selection of wavelengths:

Each working standard solution was scanned between the range 200-400 nm in 1 cm cell against blank. Maximum absorbing wavelength of CEF and PROB were selected from spectral data and isobestic wavelength selected from overlain spectra of zero order. The λ max for CEF, PROB and isobestic point was 233nm, 247nm and 242nm respectively.

Method I:

In quantitative estimation of two components by simultaneous equation method, absorbances were measured at the maximum absorption wavelengths of two drugs. From the spectra of CEF and PROB absorbances were measured at selected wavelengths i.e. 233nm (λ1) and 247nm (λ2) the maximum absorption of CEF and PROB respectively. The absorptivity coefficients of each drug at both wavelengths were determined. The concentration of each drug in laboratory mixture and tablet formulation was determined by substituting the absorbance and Absorptivity coefficient in the following sets of equations.

$$C_A = \frac{\text{Abs } \lambda_2.ay_1 - \text{Abs } \lambda_2.ay_2}{ax_2.ay_1 - ax_2.ay_2}$$

$$C_B = \frac{\text{Abs } \lambda_2.ax_2 - \text{Abs } \lambda_2.ax_1}{ax_2.ay_1 - ax_2.ay_2}$$

Where, A1 and A2 are absorbances of mixture at 208 nm and 237.5 nm respectively, ax1 and ax2 are absorptivities of CEF at λ1 and λ2 respectively and ay1 and ay2 are absorptivities of PROB at λ1 and λ2 respectively. Cx and Cy are concentrations of CEF and PROB respectively.

Method II:

In Q analysis method the absorbances were measured at the isobestic point and maximum absorption wavelength of PROB. From overlain spectra of CEF and PROB (fig) absorbance were measured at the selected wavelengths i.e. 242nm (isobestic point) and at 247nm, the maximum absorption of PROB. The absorptivity coefficients of each drug at both wavelengths were determined. The concentration of each drug in laboratory mixture and tablet formulation was determined by substituting the absorbance and absorptivity coefficients in the following sets of equations.

$$C_A = \frac{Q_M - Q_Y}{Q_X - Q_Y} \times \frac{A}{ax_1}$$

$$C_B = \frac{Q_M - Q_X}{Q_Y - Q_X} \times \frac{A}{ay_1}$$

Procedure for analysis of tablet formulation:

Twenty tablets were accurately weighed and average weight was calculated. The tablets were

triturated to a fine powder. An accurately weighed quantity of powder equivalent to 250 mg

CEF and250 mg Probenecid was dissolved in 20 ml methanol and sonicated for 20 min and volume was made up to 100ml. The solution was filtered through Whatman filter paper No 41 and aliquot portion of filtrate was diluted to produce solution having concentration of 10µ/ml of CEF and 10µ/ml of PROB. The absorbance of sample solution was measured at selected wavelengths and the concentrations of the two drugs were estimated using simultaneous equation method and absorbance ratio method. The analysis procedure was repeated six times and the results are depicted in Table 1.

Validation:

The methods were validated with respect to linearity, limit of detection (LOD), limit of

quantification (LOQ), precision, accuracy and ruggedness. To study accuracy of the developed methods, recovery studies were carried out using standard addition method at three different levels. Percent recovery and low relative standard deviation for six replicates of sample solution was less than 2%, which met the acceptance criteria established for spectrophotometric methods. Ruggedness of the proposed method was determined by analysis of sample solution prepared by proposed methods between different days. The percent relative standard deviation was found to be less than 2% showed ruggedness of the spectrophotometric methods. The results obtained are summarized in Tables.

Table 1 Linear regression analysis of calibration curves with their respective absorptivity values:

Parameter	Method First		Method Second	
	CEF	PROB	CEF	PROB
Correlation coefficient (r)	0.9978	0.9921	0.9959	0.9995
Molar Absorptivity (lit/mole/cm)	1.2202	0.0752	1.2202	0.0752
Slope	0.0421	0.0327	0.0293	0.0308
Intercept	0.0094	0.0165	0.0016	0.0092

Table 2 Results of recovery studies

Level of recovery %	Amount of pure drug added(mg)		Simultaneous equation method % recovery		Absorbance ratio method % recovery	
	CEF	PROB	CEF	PROB	CEF	PROB
80	200	200	99.44	99.72	99.40	99.67
100	250	250	99.35	99.65	99.23	99.89
120	300	300	99.50	99.72	99.89	99.56
Mean % recovery			99.43	99.69	99.23	99.56
SD*			0.75	0.040	0.34	0.16
CV**			0.75	0.040	0.034	0.016

*SD = Standard deviation ** CV = coefficient of variance

Table 3 Results of analysis of tablet formulation:

Drugs	Simultaneous equation method % ± SD(n=6)	Absorbance ratio method % ± SD(n=6)
CEF	100.01±0.017	100.06±0.015
PROB	100.02±0.088	100.02±0.012

Table 4 Results of intermediate precisions:

Day	**Method I**		**Method II**	
	% Label claim estimated (Mean ±%R.S.D*)		% Label claim estimated (Mean ±%R.S.D*)	
	CEF	PROB	CEF	PROB
Intraday	99.2±0.15	99.5±0.15	99.5±0.16	99.67±0.12
Interday	99.6±0.55	99.9±0.40	99.3±0.015	99.43±0.14

*R.S.D. = Relative standard deviation

The overlain spectra of CEF and PROB exhibit λ max of 233 nm and 247nm for CEF and PROB respectively which are quite separated from each other. Additionally one is absorptive point was observed at 243 nm. This wavelength was selected for simultaneous estimation of CEF and PROB for Q value analysis and it is assumed to be sensitive wavelength. Standard calibration curves for CEF and PROB were linear with correlation coefficients (r) values in the range of 0.9933 – 0.9956 at all the selected wavelengths and the values were average of three readings with standard deviation in the range of 0.16 – 0.34. The calibration curves were repeated three times in a day and the average % RSD was found to be 0.034 for CEF and 0.16 for PROB; similarly the method was repeated for three different days and average %

RSD was found to be 0.033 for CEF and 0.17 for PROB. The accuracy of the methods was confirmed by recovery studies from tablet at three different levels of standard additions; recovery in the range of 99.76 – 100% justifies the accuracy of method.

Conclusion:

The proposed UV spectrophotometric methods are a simple, accurate, precise, rapid and economical for the simultaneous estimation of CEF and PROB in tablet dosage form. The proposed methods use inexpensive reagents, solvents and instruments that are available in laboratories. Hence, these methods can be conveniently adopted for the routine analysis in quality control laboratories.

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References:

1. Cefadroxil. Drug Bank. [Internet] 2013 Feb [cited 2013 Oct 24]. Available from: www.drugbank.ca/drugs/DB01140
2. Shukla R, Patel A, Soni M, Modi V , Jaliwala Y. Quantitative spectrophotometric estimation of Cefadroxil using hydrotropic solubilization technique. *Asian journal of pharmaceutics*. 2008; 2:146-7.
3. Blanchin MD, Kok WT, Fabre H. New detection modes for the determination of cephalosporins and their decomposition products. *Chromatographia.* 1987 Dec; 24 (1): 625 – 27.
4. Badawy SS, Abdel-Gawad FM, Ibrahim MM. Spectrophotometric Studies on Determination of Cefadroxil with Copper(II) and Vanadium(V) in Sulphuric Acid Medium. Anal. Lett. 1993 March; 26 (3): 487-97.
5. Butler D: Wartime tactic doubles power of scarce bird-flu drug. Nature. Pubmed. 2005 Nov 3; 438(7064): 6.

Overlay Spectrum Graph Report

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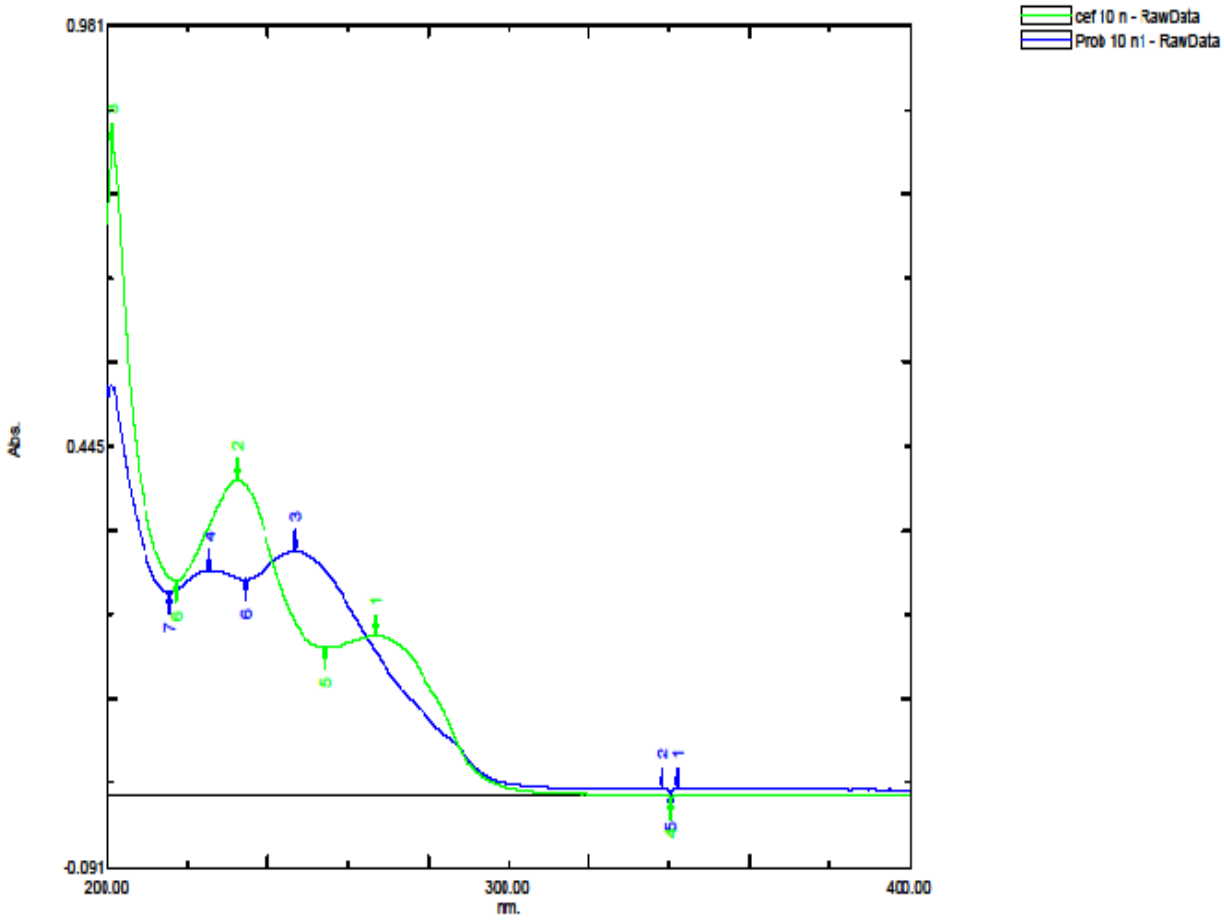

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