Spectrophotometric Estimation of Cefotaxime and Ceftriaxone in Pharmaceutical Dosage Forms

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A simple, sensitive, accurate and rapid spectrophotometric method has been developed for the estimation of cefotaxime and ceftriaxone using Folin-Ciocalteu reagent in presence of 20% sodium carbonate solution. The blue colour chromogen formed is measured at wavelength of maximum absorption 752 nm and 750 nm for cefotaxime and ceftriaxone respectively against reagent blank. The chromogen obeyed linearity over 5.0 to 60 μ g/ml for cefotaxime, and 2.0 to 36 μ g/ml for ceftriaxone. The results of analysis have been validated statistically and by recovery studies.

Chemically, cefotaxime (CFT) is (6R,7R)-3[(acetyloxy)methyl]-7-[[(2Z)-(2-amino-4-thiazolyl)(methoxyamino)acetyl]amino]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2carboxylic acid¹. Chemically, ceftriaxone (CFX) is (6R,7R)-7-[[(2Z)-(2-amino-4-thiazolyl)(methoxyamino)-acetyl]amino]-8-oxo-3-[[1,2,5,6-tetrahydro-2-methyl-5,6-dioxo-1,2,4-triazin-3-yl)-thio]methyl]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2carboxylic acid². Cefotaxime and ceftriaxone are third generation broad spectrum cephalosporins for parenteral administration and are bactericidal and mainly used in the treatment of various bacterial infections caused by Grampositive and Gram-negative micro-organisms^{3,4}. Cefotaxime is official in IP, USP and BP. The IP⁵, USP⁶ and BP7 describe HPLC method for estimation of cefotaxime. Literature survey reveals HPTLC⁸, HPLC^{9,10} and spectrophotometric methods¹¹⁻¹³ for its determination. Ceftriaxone is official in USP and BP but not official in IP. The USP¹⁴ and BP¹⁵ describe HPLC method for estimation of ceftriaxone. Literature survey reveals HPTLC⁸, HPLC⁹ and spectrophotometric methods^{11,12} for its determination. The present communication describes a simple, sensitive, accurate, rapid and economical colorimetric method for the estimation of CFT and CFX in their dosage forms using Folin-Ciocalteu (FC) reagent in presence of 20% sodium carbonate solution.

A Shimadzu model 1601 double beam UV/Vis spectrophotometer with spectral width of 2 nm and wavelength accuracy of 0.5 nm and with a pair of 10 mm matched quartz cells was used to measure absorbance of the resulting solutions. A Sartorius CP224S analytical balance, an ultrasonic cleaner (Frontline FS 4), cefotaxime and ceftriaxone (Mann Pharmaceuticals Ltd., Mehsana), FC reagent (diluted to 1:4 with glass-distilled water), 20% sodium carbonate solution and double glass-distilled water were used in the study.

The standard stock solution of CFT and CFX were prepared by dissolving CFT and CFX, 10 mg of each, in 100 ml volumetric flask separately using glass-distilled water (100 μ g/ml). Aliquots of 0.5 to 6.0 ml portions of standard solution of cefotaxime and 0.2 to 3.6 ml of ceftriaxone were transferred to a series of 10 ml corning volumetric flask. To each flask, 1 ml and 2 ml of 20% sodium carbonate solution with 1.5 ml and 3 ml of diluted FC reagent for cefotaxime and ceftriaxone respectively were added. After thoroughly shaking, the flasks were set aside for 10 min for the reaction to complete. The volumes of each flask were adjusted to 10 ml with glass-distilled water. The absorbance of solution in each flask was measures at 752 nm and 750 nm for cefotaxime and ceftriaxone, respectively against reagent blank.

An accurately weighed powder equivalent to 10 mg each of cefotaxime and ceftriaxone was transferred to separate 100 ml volumetric flasks. The content was dissolved in glass-distilled water and diluted up to the mark with glassdistilled water. These solutions were then analyzed, as described, under respective calibration curve procedure. The analysis procedure was repeated five times with pharmaceutical formulation and the result of analysis of pharmaceutical formulation is shown in Table 1.

To study the accuracy and precision of the proposed method, recovery studies were carried out by addition of known amount of standard drug solution of CFT and CFX to pre-analyzed formulation. The resulting solution was then reanalyzed by proposed method. Results of recovery studies were found to be satisfactory and are reported in Table 1.

In the present work, the quantitative reaction of the drug with FC reagent is proposed. The reaction is based on the reduction of phosphomolybdotungstic acid, the FC reagent, by cefotaxime and ceftriaxone in presence of 20% sodium carbonate solution, thereby producing reduced species having characteristic blue colour with maximum absorption at 752 nm and 750 nm respectively. It was found that 1.5 ml FC reagent with 1 ml 20% sodium carbonate solution for cefotaxime and 3 ml FC reagent with 1.5 ml 20% sodium carbonate solution for ceftriaxone was sufficient for the development of maximum colour intensity. Colored chromogen was found to be stable for more than 3 h at room temperature for both the drugs. The linearity was found in the concentration range of 5 to 60 μ g/ml (r²=0.9944) for cefotaxime and 2 to 36 μ g/ml (r²=0.9926) for ceftriaxone. The reproducibility, repeatability and accuracy of the method are very good,

Formulation (Injection)	Labelled claim (mg/vial)	Amount found* (mg/vial)	% Claim* ± S.D	% Recovery* ± S.D
CFT1	250	248.2	99.3±0.73	101.3±0.63
CFT2	1000	988.9	98.9±0.62	100.1±0.49
CFT3	500	506.8	101.4±0.67	99.7±1.18
CFX1	250	249.2	99.7±0.38	101.4±0.65
CFX2	1000	1006	100.6±0.52	99.3±0.91
CFX3	500	493.8	98.8±1.03	100.5±0.76

TABLE 1: ANALYSIS OF PHARMACEUTICAL FORMULATIONS

*Mean of five determinations, CFT- Cefotaxime, CFX- Ceftriaxone

TABLE 2: OPTICAL CHARACTERISTICS ANDPRECISION OF THE PROPOSED METHOD

Cefotaxime	Parameters	Ceftriaxone
752	λ-max (nm)	750
5-60	Linearity range (µg/ml)	2-36
0.9944	Correlation coefficient	0.9926
1.1568x10⁴	Molar extinction coefficient	2.3847x10⁴
	(l/mol.cm)	
0.03937	Sandell's sensitivity	0.02326
	(µg/cm ² /0.001 A.U.)	
±0.765	% Relative standard deviation (CV)	±0.983
±0.003489	Standard deviation (S.D)	±0.004586
±0.001561	Standard error of mean (S.E.M)	±0.002051
	Regression equation (y*)	
0.0202	Slope (a)	0.0276
0.0595	Intercept (b)	0.1028

 $y^* = b+ac$ Where 'c' is the concentration and y is absorbance unit.

as shown by the low values of standard deviation and coefficient of variation (C.V). The percentage recovery value in the range of 99.7 to 101.3% for cefotaxime and 99.3 to 101.4% for ceftriaxone indicates non-interferences from the formulation excipients. All the validated parameters are summarized in Table 2.

In conclusion, the proposed method is new, simple, sensitive, accurate and precise and can be successfully employed for the routine analysis of these drugs in pharmaceutical dosage form (dry powder for injection).

Budavari, S., Eds., In; The Merck Index. 13th Edn., Merck & Co., Inc., Whitehouse Station. NJ, 2001, 330.

- 2. Budavari, S., Eds., In; The Merck Index. 13th Edn., Merck & Co., Inc., Whitehouse Station. NJ, 2001, 335.
- 3. Mishra, L., Eds., In; Drug Today. March-June-2003, Vol. II, No. 4, Lorina Publications Inc. Delhi. 231.
- 4. Mishra, L., Eds., In; Drug Today. March-June-2003, Vol. II, No. 4, Lorina Publications Inc. Delhi. 233.
- Indian Pharmacopoeia, Vol. I, Government of India, The Controller of Publications, Delhi, 1996, 148.
- 6. The United States Pharmacopoeia, 26th Revision, U.S. Pharmacopoeial convention, Inc., Rockville, M.D., 2003, 369.
- 7. British Pharmacopoeia, Vol. I, Her Majesty's Stationary Office, London, 2000, 321.
- Eric, J.S., Agbaba, D., Zivanov-Stakik, D. and Vladirnirow, S., J. Pharm. Biomed. Anal., 1998, 18, 893.
- 9. Joshi, S., J. Pharm. Biomed. Anal., 2002, 28, 795.
- Shindee, V.M. and Shabadi, C.V., Indian. J. Pharm. Sci., 1998, 60, 313.
- 11. Al-Momani, I.F., J. Pharm. Biomed. Anal., 2001, 25, 751.
- 12. El-Walily, A.F.M., Gazy, A.A., Belal, S.F. and Khamis, E.F., J. Pharm. Biomed. Anal., 2000, 22, 385.
- 13. Nuevas, L., Gonzalez, R., Rodrguez, J.C. and Hoogmartens, J., J. Pharm. Biomed. Anal., 1998, 18, 579.
- 14. The United States Pharmacopoeia, 26th Revision, U.S. Pharmacopoeial convention, Inc., Rockville, M.D., 2003, 386.
- 15. British Pharmacopoeia, Vol. I, Her Majesty's Stationary Office, London, 2000, 329.

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REFERENCES