Development and Validation of Spectrophotometric and Hplc Methods for the Determination of Cefixime in Capsule and Suspension

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Abstract: Cefixime is an oral third generation cephalosporin antibiotic. It is used to treat gonorrhea, tonsilitis and pharyngitis. Two simple, rapid and selective methods were developed for the determination of cefixime in drug substance and its pharmaceutical preparations. The first method (I) is based on charge transfer complex formation between cefixime (CF) with 7,7,8,8-tetracyanoquinodimethane (TCNQ) and I₂ reagents in acetonitrile and 1,2-dichloromethane, respectively. Where coloured charge transfer complexes were obtained and measured spectrophotometrically at 842 and 360 nm, respectively. All variables affecting the reaction were investigated and the conditions were optimized. Beer's law was obeyed over the concentration range from 10 to 240 and 0.25 to 17.5 µg mL⁻¹ for TCNQ and I₂ reagents, respectively. The molar ratio of the formed CF-TCNQ CT complexes are found to be 1:1 as deduced by Job's method where the molar ratio of the formed CF-I₂ CT complexes are found to be 2:3. The Lower Detection Limits (LOD) and the limits of quantification (LOQ) were found to be 1.10 and 3.80 and 3.21 and 1.07 µg mL⁻¹ for TCNQ and I₂ reagents, respectively. A high performance liquid chromatography (HPLC; method II) was used for CF determination in capsule and suspension forms. The method is based on separation of CF on a reversed phase, Waters, Symmetry C18 column (5 µm, 250x4.6 mm) using a mobile phase consists of a mixture of water, acetonitrile and glacial acetic acid and adjusted to pH 2 using orthophosphoric acid (72: 25: 3 (v/v/v)) at a flow rate of 1.5 mL min⁻¹ at ambient temperature with UV detection at 273 nm. The procedure provided a linear response over the concentration range from 1 to 500 µg mL⁻¹ with a mean accuracy of 100.9%±0.728. The LOD and LOQ were 0.432 and 1.439 µg mL⁻¹, respectively. The proposed methods were successfully applied for the determination of cefixime in bulk powder and in dosage forms. There was no significant difference between each of the two methods and the official one.

Key words: Cefixime, spectrophotometry; 7, 7, 8, 8-tetracyanoquinodimethane, i₂, hplc, pharmaceutical preparations

INTRODUCTION

Cefixime (CF), has the IUPAC name sodium (Z)-7-[2-(2-aminothiazole-4-yl)-2-(carboxymethoxyimino)acetamido]-3-vinyl-3-cephem-4-carboxylic acid trihydrate. Its structure is given in Fig. 1. It has the molecular formula C₁₆H₁₅N₅O₇S₂·3H₂O and its molecular weight is 507.5 g mol⁻¹. It occurs as a white to light yellow crystalline powder. Practically insoluble in water, in ether, in ethyl acetate and in hexane, slightly soluble in alcohol, in acetone and in glycerol, soluble in methyl alcohol and in propylene glycol. pH of a solution in water containing the equivalent of cefixime (0.07%) is between 2.6 and 4.1. It must be stored in airtight containers.

Literature survey revealed many chromatographic methods for determination of Cefixime alone or in combinations with other drugs from pharmaceutical

formulations and biological fluids (Jovanovic *et al.*, 1998; Al-Momani, 2001; Fattah *et al.*, 2000; Meng *et al.*, 2005; Nemutlu *et al.*, 2009; Dhoka *et al.*, 2010; Zendelovska *et al.*, 2003; Raj *et al.*, 2010; Deshpande *et al.*, 2010; Kumudhavalli *et al.*, 2010). Several cyclic voltammetric (Jain *et al.*, 2010; Golcu *et al.*, 2005; Reddy *et al.*, 2003) and spectrophotometric (Shah and Pundarikakshudu, 2006; Maheshwari, 2005) methods have also been reported for determination of cefixime in pharmaceutical formulations and biological fluids. The present study aims chiefly to develop spectrophotometric (method I) and HPLC (method II) methods for the determination of CF in capsule and suspension without any interference from the excipients. Different experimental conditions were optimized and Beer's law was obeyed. The suggested procedures were compared statistically with the official method using the

Fig. 1: Structure of cefixime drug

t- and F- ests. The recovery values obtained indicate no significant differences between the suggested methods and the official method. It also indicates the possibility of applying the suggested procedures in routine analysis of CF in capsule and suspension.

MATERIALS AND METHODS

Materials and reagents: All chemicals and reagents were of analytical grade except otherwise specified and solutions were made with doubly distilled water. Cefixime reference standard and bulk powder was supplied from Sigma, Egypt. Cefixime bulk powder was used as working standard and its purity was found to be 99.99% according to the manufactured method [Sigma, Egypt]. 7,7,8,8-tetracyanoquinodimethane (TCNQ) (purchased from Aldrich) and iodine (I_2) (purchased from El-Nasr company, Egypt) reagents were used. 0.02% (w/v) of TCNQ reagent was prepared by dissolving the accurate weighed amount of 20 mg of TCNQ in 100 mL acetonitrile and 0.05% (w/v) I_2 was prepared by dissolving 50 mg in 100 mL methanol in a calibrated measuring flask. The used pharmaceutical preparations included CF were Ximacef suspension (labeled to contain 100 mg/5 mL suspension was supplied from Sigma, Egypt) and Hebixime capsule (labeled to contain 400 mg/capsule and it was manufactured by Shifa Medical Products (Simco), Egypt).

Instrumentation: Shimadzu (UV-1601) UV-visible spectrophotometer with quartz cells of 1 cm optical length incorporated with a pc computer was used. HPLC instrument equipped with agilent 1100 quaternary pump, Agilent 1100 variable wavelength detector (UV-VIS detector), Agilent 1100 thermostatted column compartment (Waters, Symmetry C18, 5 μ m, 250 $\times$ 4.6 mm, column), Agilent 1100 series vacuum degasser and injector (20 μ L loop) was used.

Standard solutions: For methods I, 1.97×10^{-3} and 1.97×10^{-4} mol L^{-1} of CF solutions were prepared by dissolving the accurate weighed amount in a definite volume of methanol to get the required concentration. The

solutions were used for carrying out the reaction with TCNQ and I_2 , respectively. For method II, stock solution of CF was prepared by dissolving 100 mg of the drug in 100 mL of methanol (HPLC grade) in a calibrated measuring flask. Dilute solutions were prepared by accurate dilution from the stock one by the mobile phase.

Sample preparation: Five intact capsules of Hebixime drug were accurately emptied and the average weight of one capsule was calculated. A portion of the powder equivalent to 1 mg of the active material was dissolved in 100 mL of methanol (HPLC) grade. The resulting solutions were stirred well using magnetic stirrer for 10 min.

Accurately the powder of Ximacef suspension was weighed and divided by 12 (the number of doses) to get the weight of one dose which is equivalent to 100 mg of CF. A portion of the powder equivalent to 1 mg of the active material was dissolved in 100 mL of methanol (HPLC) grade. The resulting solutions were stirred well using magnetic stirrer for 30 min.

Chromatographic conditions: The mobile phase was composed of water, acetonitrile and glacial acetic acid mixture (72:25:3 (v/v/v)) and adjusted to pH 2 using orthophosphoric acid. It was sonicated, filtered by using a 0.45 μ m nylon membrane filter and degassed by ultrasonic vibrations. The flow rate was set at 1.5 mL min^{-1} using a reversed phase, Waters, Symmetry C18 column (5 μ m, 250 $\times$ 4.6 mm) and UV detection at 273 nm. All determinations were performed at ambient temperature (25 $^{\circ}C$) and the injection volume was 20 μ L.

Procedures: Calibration for spectrophotometric method. Series of solutions were prepared in which the concentration of the reagent was kept constant (2.5 mL of 0.02% (w/v) of TCNQ and 2 mL of 0.053 % (w/v) of I_2), while that of the drug was regularly varied from 0.05 to 3 mL of 1 mg mL^{-1} drug solution, then the solution was completed to 5 mL with acetonitrile and 10 mL with 1,2 dichloromethane for TCNQ and I_2 reagents, respectively. After the selected time for each complex formation, the CT complex was formed and the absorbance values were measured at the specified λ_{max} for each complex, against a blank solution. For more accurate analysis; Ringbom ⁽²⁾ plots (Ringbom, 1939) had been drawn by plotting log [drug] in μ g mL^{-1} versus percent transmittance and the linear portion of the S-shaped curve gave the accurate range of analysis.

Calibration for HPLC method: Aliquots of CF drug solution (1 mg mL^{-1}) in the concentration range from 1.0 to 500 μ g mL^{-1} were transferred into 10 mL volumetric

flasks and completed to the mark with the mobile phase solvent. Triplicate 20 μ L of each solution were injected using the above chromatographic conditions. The calibration curve was constructed versus the corresponding concentrations of CF and the regression equation was computed.

Application to capsule and suspension: The above procedures were applied to the analysis of Ximacef suspension and Hebixime capsule, using sample preparation as mentioned under 'sample preparation'. The concentration of CF was calculated from the recorded regression equations.

RESULTS AND DISCUSSION

Spectrophotometric method: This study is undertaken in the view that, CT complexes are formed between the amino group of CF drug and TCNQ or I_2 reagents via the protonated nitrogen atom of the drug. On adding basic drug solution to TCNQ or I_2 , stable coloured CT complexes are formed. The absorption spectra of the formed CT complexes in acetonitrile and 1,2-dichloromethane, respectively are scanned against blank reagent in the wavelength range from 300-900 nm and from 300-450 nm, respectively and the results obtained are represented graphically in Fig. 2a, b. These figures show

Fig. 2(a-b): Absorption spectrum of (a) CF-TCNQ CT complex in acetonitrile and (b) CTX- I_2 CT complex in methylene chloride

that the CT complexes attain their maxima at 842 and 360 nm for CF with TCNQ and I_2 reagents, respectively. Different factors affecting the formation of the coloured CT complexes are studied carefully in order to select the optimum conditions necessary for determination of CF drug in pure form and in pharmaceutical preparations. These factors include the effect of solvents, time, temperature, reagent concentration and the stoichiometry of the reactants.

Several organic solvents as methanol, 1,2-dichloroethane, chloroform, 1,4-dioxane, acetonitrile and acetone were tried. Acetonitrile and 1,2-dichloromethane were found as the most suitable media for the formation of CT complexes as indicated by the high molar absorptivity values using TCNQ ($\epsilon = 2.3 \times 10^3 \text{ L mol}^{-1} \text{ cm}^{-1}$ at $\lambda = 842 \text{ nm}$) and I_2 ($\epsilon = 1.32 \times 10^4 \text{ L mol}^{-1} \text{ cm}^{-1}$ at $\lambda = 360 \text{ nm}$) reagents, respectively.

The effect of time on the formation and stability of the CT complexes is studied carefully and the results are illustrated in Fig. 3. The absorbance values remain almost unchanged with the increase of time. The optimum time for the completion of the reaction of CF with TCNQ and I_2 reagents is 60 and 30 min, respectively. The results indicate that CT complexes need the mentioned time for their complete formation. The intensity of the colour formed after formation of CT complexes by the suitable solvent is stable for at least 24 h.

The absorbance of the formed CT complexes is measured at temperatures ranged from 0 to 60°C. The results show that, 60 and 20°C are the most suitable temperatures for the formation and stability of the complex then the absorbance is suddenly decreased with the increase in temperature using TCNQ or I_2 reagents, respectively. Therefore, the mentioned temperatures are chosen as the best temperature for determination of the drug under study in pure and in pharmaceutical formulations.

The effect of varying the concentrations of TCNQ and I_2 reagents were studied. The CF concentration is

Fig. 3: Effect of time on the absorbance of CT complexes of CF with a) TCNQ and b) I_2

Scheme 1: Structure of CF-TCNQ CT complex

Scheme 2: Structure of CF-I₂CT complex

kept constant at 1 mg mL⁻¹, while the concentrations of TCNQ (0.02%) and I₂ (0.053%) reagents are varied from 0.2-4 mL. It is found that the absorbance of the formed CT complexes increased by increasing the TCNQ or I₂ concentrations till 2.5 and 2 mL, respectively. Above this volume, the absorbance remains constant even with further addition of the reagents. So any excess of reagents has no effect on the determination of CF drug.

The composition of CT complexes was established by applying the continuous variation (Job, 1928) and the molar ratio (Yoe and Jones, 1944) methods. The results indicate that 1:1 [drug]: [Reagent] for CF-TCNQ and 2:3 [Drug]: [Reagent] for CF-I₂ CT complexes are formed with the investigated drug (Pandeewaran and Elango, 2009; Zayed and El-Habeeb, 2009).

The validity of Beer's law for the formed CT complexes through the reaction of the drug under study with TCNQ and I₂ reagents, method is shown in Fig. 6. The calibration curves are rectilinear over the

concentration range of 10-240 and 0.25-17.5 µg mL⁻¹ for CF drug using TCNQ and I₂ reagents (Table 1). For more accurate results, Ringbom optimum concentration range is obtained for the drug under investigation (Scheme 1 and 2).

HPLC method: A simple HPLC method is adopted for the determination of CF drug in bulk powdered or in pharmaceutical dosage forms. Different systems of mobile phases are tried using variable organic and inorganic solvents with different ratios and different pHs such as methanol and phosphate buffer, acetonitrile and phosphate buffer and methanol, acetonitrile and phosphate buffer. The best one is found to be an isocratic RP-HPLC system using C18 analytical column with (72: 25: 3 (v/v)) mixture of water, acetonitrile and glacial acetic acid and adjust to pH 2 using orthophosphoric acid. Ultraviolet detection at 273 nm gives excellent determination of CF. This system gives an excellent resolution and sensitivity. Chromatogram is well defined, resolved, symmetric and free of tailing. Under the specified chromatographic conditions, the main peak of CF (100 µg mL⁻¹) eluted at retention time of about 2.246 min Fig. 4.

Table 1: Validation report of spectrophotometric and HPLC methods for the determination of CF

Parameters	Method I		Method II HPLC
	TCNQ	I _b	
Linearity range ($\mu\text{g mL}^{-1}$)	10-240	0.25-17.5	1-500
Regression equation	$0.920 X + 0.462$	$0.328 X - 0.008$	$19234 X + 88.59$
Slope	0.920	0.328	19234
Intercept	0.462	0.008	88.59
Correlation coefficient (r)	0.999	0.999	0.999
SD	0.04-0.06	0.03-0.007	0.829
RSD (%)	0.02-0.12	0.060-1.19	0.669
Limit of detection ($\mu\text{g mL}^{-1}$)	1.10	3.80	3.21
Limit of quantification $\mu\text{g mL}^{-1}$	1.07	0.432	1.439

Fig. 4: HPLC chromatogram of $100 \mu\text{g mL}^{-1}$ cefixime working standard

Methods validation

Linearity: The linearity of an analytical method is its ability to elicit test results that are directly, or by a well-defined mathematical transformation, proportional to the concentration of analyte in samples within a given range (United States Pharmacopeial Convention, 2000). For method II, linearity was evaluated by injecting $20 \mu\text{L}$ standard concentrations of CF in the range of 1.0 to $500 \mu\text{g mL}^{-1}$ under the optimum chromatographic conditions where the peak area obtained versus the corresponding concentration of CF are plotted to construct the calibration curves (Fig. 5a, b) and linear regression analysis of CF was driven in Table 1.

The Limit of Quantification (LOQ) was determined by establishing the lowest concentration that can be measured according to ICH Q2B. The Limits of Detection (LOD) were determined by establishing the minimum level at which the analyte can be reliably detected and the results are summarized in Table 1. LOQ and LOD were calculated according to the following equation:

$$\text{LOQ} = 10 \sigma/S$$

$$\text{LOD} = 3.3 \sigma/S$$

where, σ is the standard deviation of the intercept of the regression line. S is the slope of the calibration curve.

Fig. 5: Linearity of the peak area to the concentration of CF by the proposed HPLC method.

Precision: The precision of an analytical method is the degree of agreement among individual test results when the method is applied repeatedly to multiple homogenous samples (United States Pharmacopeial Convention, 2000).

Repeatability:

(a) Method repeatability: A batch of CF bulk powder is analyzed six times by preparing six solutions with final concentration of $100 \mu\text{g mL}^{-1}$. These solutions are chromatographed against the reference standard according to the chromatographic condition described before. The results obtained are shown in Table 2.

(b) Injection repeatability: Multiple injection of homogenous sample with final concentration of $100 \mu\text{g mL}^{-1}$ CF drug indicates the performance of the HPLC instrument under chromatographic condition and day tested. The data obtained are shown in Table 3.

Ruggedness: The ruggedness of the method is carrying out by changing the experimental condition such as, changing to another stationary phase of similar type C18 and changing the flow rate and chromatographic patterns

Table 2: Repeatability data for the analysis of pure samples of CF by the proposed HPLC method

Sample No.	Concentration ($\mu\text{g mL}^{-1}$)		Recovery (%)
	Taken	Found	
1	100.0	99.81	99.81
2	100.0	99.54	99.54
3	100.0	101.2	101.2
4	100.0	100.5	100.5
5	100.0	100.7	100.7
6	100.0	101.4	101.4

Mean peak area = 2312.35 RSD % = 1.533

Table 3: Injection repeatability data assay of CF by the proposed HPLC method

Sample No.	peak area
1	2373.37329
2	2241.19897
3	2302.61792
4	2325.52393
5	2314.54956
6	2293.16553
7	2305.09131
8	2310.02002
9	2303.75830
10	2354.20557

Mean peak area = 2312.35 RSD % = 1.533

Table 4: Day-by-Day analysis results of CF by the proposed HPLC method

(CF) Taken ($\mu\text{g mL}^{-1}$)	Day (1)				Day (2)			
	(CF) Found ($\mu\text{g mL}^{-1}$)	Recovery (%)	Average Recovery (%)	RSD (%)	(CF) Found ($\mu\text{g mL}^{-1}$)	recovery (%)	Average recovery (%)	RSD (%)
80.00	81.13	101.4	100.1	1.23	80.88	101.1	98.48	0.735
	79.99	99.99			80.44	100.5		
	79.18	98.97			79.71	99.64		
100.0	99.54	99.54	101.2	1.66	98.95	98.95	100.5	0.589
	101.2	101.2			99.36	99.36		
	102.9	102.9			98.23	98.23		
120.0	118.6	98.81	100.6	1.59	121.4	101.1	101.1	0.411
	122.4	102.0			122.0	101.7		
	121.1	100.9			120.5	100.5		

Day 1: n = 9, mean percentage recovery (%) = 100.6%, RSD = 1.39, Day 2: n = 9, mean percentage recovery (%) = 100.1%, RSD = 1.144

Table 5: Column-Column analysis results of CF by the proposed HPLC method

(CF) Taken ($\mu\text{g mL}^{-1}$)	Day (1) Waters, Symmetry C18, 5 μm , 250x4.6mm dimensions				Day (2) Thermo, BDS Hypersil C18, 5 μm , 250x4.6mm dimensions			
	(CF) Found ($\mu\text{g mL}^{-1}$)	Recovery (%)	Average Recovery (%)	RSD (%)	(CF) Found ($\mu\text{g mL}^{-1}$)	recovery (%)	Average recovery (%)	RSD (%)
80.00	80.88	101.1	98.48	0.735	81.71	102.1	101.3	0.728
	80.44	100.5			80.81	101.0		
	79.71	99.64			80.60	100.8		
100.0	98.95	98.95	100.5	0.589	100.0	100.0	99.69	1.163
	99.36	99.36			100.7	100.7		
	98.23	98.23			98.41	98.41		
120.0	121.4	101.1	101.1	0.411	122.3	101.9	101.2	0.807
	122.0	101.7			121.8	101.5		
	120.5	100.5			120.4	100.3		

Column 1: n = 9, mean percentage recovery = 100.0%, RSD (%) = 1.14, Column 2: n = 9, mean percentage recovery = 100.7%, RSD (%) = 1.11

were studied. It also established through the studies on the reaction solutions by different persons on the same chromatographic system. (a) Day-by-Day reproducibility Sample solutions (80, 100 and 120 $\mu\text{g mL}^{-1}$) are analyzed on each of two days using the same instrument and column. Results obtained are shown in Table 4. (b) Column-Column reproducibility Sample solutions (80, 100 and 120 $\mu\text{g mL}^{-1}$) are analyzed on each of two different columns using the same instrument. Results obtained are shown in Table 5.

Accuracy: Accuracy of the two forms is checked by applying the standard addition technique by preparing sample solutions ranging from (20-250 $\mu\text{g mL}^{-1}$) (Fig. 6). The specified chromatographic procedure is then performed and the recovery results are shown in Table 6.

Pharmaceutical applications: The validity of the proposed methods is examined for the determination of CF drug in dosage forms namely Ximacef suspension and Hebixime capsule (Table 8). The concentration of the drug in the dosage forms is calculated from the appropriate calibration graphs. There is no shift in the absorption maximum due to the presence of other constituents of the suspension forms. The results of determination of CF drug using TCNQ and I_2 reagents and HPLC method in

Table 6: Accuracy data for the analysis of CF in Ximacef (100 mg\5mL suspension) and Hebixime (400 mg capsule) by the proposed HPLC method

[CF] Taken ($\mu\text{g mL}^{-1}$)	[CF] Found ($\mu\text{g mL}^{-1}$)		Recovery (%)	
	Ximacef*	Hebixime [#]	Ximacef	Hebixime
20.00	19.83	19.59	99.19	97.94
40.00	40.02	39.56	100.0	98.91
60.00	59.45	59.04	99.01	98.40
80.00	79.88	78.65	99.85	98.32
100.0	102.9	98.46	102.9	98.46
120.0	118.1	118.8	98.38	98.98
140.0	140.8	139.9	100.5	99.90
160.0	161.0	160.3	100.6	100.2
180.0	181.8	178.7	101.0	99.23
200.0	197.8	201.1	98.88	100.6
250.0	251.3	248.5	100.5	99.38

*Mean recovery = 100.1, SD = 0.427 and RSD (%) = 0.427, [#] Mean recovery = 99.12, SD = 0.441 and RSD (%) = 0.445

Table 7: Statistical analysis of determination of CF drug in different pharmaceutical preparations using TCNQ and I₂ reagents compared with the reported method

Samples	[Drug], Taken ($\mu\text{g mL}^{-1}$)	[Drug], Found ($\mu\text{g mL}^{-1}$)	Mean recovery (%) $\pm$ SD ^(a)	RSD (%)
Using TCNQ: Ximacef	60.00	59.80	99.66 $\pm$ 0.03	0.05
100 mg/5 mL suspension	140.0	138.0	98.57 $\pm$ 0.04	0.03
Hebixime 400mg Capsule	60.00	59.90	99.83 $\pm$ 0.06	0.10
	140.0	139.0	99.29 $\pm$ 0.11	0.08
Using I ₂ : Ximacef	3.50	3.48	99.42 $\pm$ 0.03	0.86
100 mg/5 mL suspension	6.00	5.93	98.83 $\pm$ 0.04	0.68
Hebixime	3.50	3.53	100.86 $\pm$ 0.02	0.57
400 mg Capsule	6.00	6.05	100.83 $\pm$ 0.05	0.83
Using Official method:				
Ximacef 100 mg/5mL suspension	100.0	99.24	99.24 $\pm$ 0.06	0.06
Hebixime 400 mg Capsule	100.0	100.3	100.3 $\pm$ 0.07	0.07

Table 8: Determination of CF drug in Ximacef (100 mg/5 mL suspension) and Hebixime (400 mg capsule) using proposed and comparison methods

Asamples (100 $\mu\text{g mL}^{-1}$)	[CF] Found $\mu\text{g mL}^{-1}$		% Recovery	
	Proposed Method	Comparison Method (HPLC)	Proposed Method	Comparison Method (HPLC)
Ximacef 100 mg/5mL suspension	99.17	99.24	98.17	99.24
Hebixime 400mg capsule	99.71	100.3	99.71	100.3

Table 9: Statistical comparison between the results obtained by the proposed HPLC and the comparison method for the analysis of CF (100 $\mu\text{g mL}^{-1}$) drug in Ximacef (100 mg/5mL suspension) and Hebixime (400 mg/capsule)

Samples (100 $\mu\text{g mL}^{-1}$)	[Drug] Found ($\mu\text{g mL}^{-1}$)	Mean recovery % $\pm$ SD ^(a)	t-test* (2.23)	F-test* (5.05)
Using proposed method: Ximacef 100 mg/5 mL suspension	98.17	98.17 $\pm$ 0.737	0.900	0.128
Hebixime 400mg/ capsule Using Official method:	99.71	99.71 $\pm$ 0.921	2.174	3.839
Ximacef 100mg/5mL suspension	99.24	99.24 $\pm$ 2.06		
Hebixime 400mg/ capsule	100.3	100.3 $\pm$ 0.47		

*The theoretical tabulated values of F and t test at 95% confidence limit

Fig. 6: HPLC chromatogram of (a) 100 $\mu\text{g mL}^{-1}$ of CF in Ximacef (100 mg\5mL suspension) and (b) 100 $\mu\text{g mL}^{-1}$ Hebixime (400 mg capsule)

both suspension and capsule forms are compared with those obtained by applying the reported method (Shah and Pundarikakshudu, 2006). The comparison method is based on HPLC-RP separation of CF with HPLC detection for Ximacef (100 mg/5 mL suspension)

and Hebixime (400 mg capsule) (using a mobile phase of (0.05 M) potassium di hydrogen o-phosphate (pH = 3): methanol (78:22 v/v) with 2 mL min⁻¹ flow rate at UV detection 286 nm). The results obtained (Table 7) are compared statistically by the % recovery with those

obtained by reported method on samples of the same batches. The values did not exceed the theoretical tabulated values indicating that there is no significant difference between accuracy of the proposed and the reported methods. HPLC chromatograms for the determination of CF in Ximacef (100 mg/5 mL suspension) and Hebixime (400 mg capsule) are shown in Fig. 6 and Table 9.

CONCLUSIONS

The presented study describes validated spectrophotometric and HPLC methods for the assay of CF. The two suggested methods are simple, selective, accurate and can be used for the routine quality control analysis of the cited drug in bulk powder and in dosage form without any interference from common excipients. The developed HPLC method allows the quantification of the drug in both pharmaceutical formulations suspension and capsule in a short analytical time.

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