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Direct Spectrophotometric Determination of Cefuroxime Axetil in Pure Form and Pharmaceutical Dosage Forms

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ABSTRACT

A simple, direct and cost-effective spectrophotometric method for determination of cefuroxime axetil (CRXA) in pure and tablet dosage forms was applied. This method is based on formation of ion-pair complex ([CRXA]:[BTB]) between CRXA and bromothymol blue (BTB) in chloroform. Beer's law in the optimum experimental conditions using [CRXA]:[BTB] complex is valid within a concentration range of 2.00-50.00 µM (1.021–25.524 µg.mL^{-1}). The developed method is applied for the determination of CRXA in pure and its commercial tablets without any interference from excipients with average assay of 96.8 to 101.6% and the results are in good agreement with those obtained by the HPLC reference method. Associated drugs (sulbactam and linesolid) with cefuroxime axetil are considered to be interfere, while metronidazole can be considered as non-interfere.

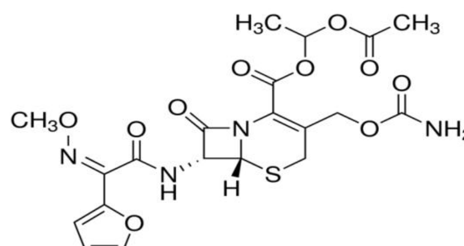
Keywords: Cefuroxime axetil; Bromothymol blue; Ion-pair complex; Direct spectrophotometric method.

1. INTRODUCTION

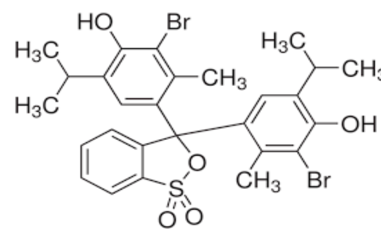
Chemically cefuroxime axetil (CRXA) is (RS)-1-hydroxyethyl (6R,7R)-7-[2-(2-furyl) glyoxyl-amido]-3-(hydroxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]-oct-2-ene-2-carboxylate,72-(Z)-(O-methyl-oxime), 1-acetate 3-carbamate], its trade name is Ceftin, mol. mass of CRXA is 510.475 g/mol and 424.38 g/mol for cefuroxime (CRX), see Scheme 1 [1]. It is a broad spectrum, semi synthetic cephalosporin antibiotics which is administered for treating variety of bacterial infections such as case of pharyngitis, chronic bronchitis and infection of urinary tract as well as uncomplicated. It is a second generation cephalosporin and can be administered orally as well as in the parenteral dosage form. The mode of action of cefuroxime against the bacteria is upon inhibiting the bacterial wall synthesis by binding to one or many penicillin binding proteins [1,2].

Bromothymol blue $C_{27}H_{28}Br_2O_5S$ (BTB), acts as a weak acid in solution. It can thus be in protonated or deprotonated form, appearing yellow or blue, respectively. It is bluish green in neutral solution. The deprotonating of the neutral form results in a highly conjugated structure, accounting for the difference in colour. An intermediate of the deprotonating mechanism is responsible for the greenish color in neutral solution, mol. mass of 624.38 g/mol [3], see scheme 2. Bromothymol blue has been used as a reagent to form ion pair complexes with drugs [4].

Scheme 1: Chemical structure of cefuroxime axetil (CRXA).



Scheme 2: Chemical structure of Bromothymol blue **(BTB).**



Various spectrophotometric [5-22], High Performance Liquid Chromatographic (HPLC), Reversed-phase high performance liquid chromatography (RP-HPLC), high performance thin layer chromatographic (HPTLC), micellar liquid chromatographic (MLC) [23-37] and voltammetric [38,39] methods have been reported for the determination of cefuroxime.

Three simple accurate spectrophotometric methods have been developed for the estimation of cefuroxime axetil in bulk drug and its solid dosage forms. Method (A) was described about UV spectrophotometric measurement at maximum absorption of 277 nm while method (B) related to formation of green colored chromogen by utilizing the oxidative coupling reaction between 3-Methyl-2-benzothiozolidine hydrazone (MBTH) and cefuroxime axetil in presence of ferric chloride. It was measured at 624 nm against reagent blank. Method (C) was based on the formation of pink colored chromogen with para dimethyl amino cinnamaldehyde (PDAC) and it was measured at 537 nm. The beer's law obeyed at the concentration of 5-25 µg.mL^{-1} , 1-5 µg.mL^{-1} and 2-10 µg.mL^{-1} for method A, B and C respectively. The developed analysis could be considered successfully for the determination of cefuroxime axetil in pharmaceutical formulation [17].

A simple, sensitive, accurate, precise and reproducible UV spectrophotometric method for determination of cefuroxime axetil using methanol as solvent was studied. In this method the simple UV spectrum of cefuroxime axetil in methanol was obtained which exhibits absorption maxima (λ_{max}) at 278 nm. The quantitative determination of the drug was carried out at 278 nm and Beer's law was obeyed in the range of (0.80-3.60) µg.mL^{-1}. Proposed method was precise, accurate and cost effective [18].

A rapid and reproducible high performance liquid chromatographic method has been developed for the estimation of CRXA in its pure form as well as in pharmaceutical dosage forms. Chromatography was carried out on an ODS C18 column (150 x 4.6 mm x 5 µm length), using a mixture of methanol and 0.01M potassium dihydrogen orthophosphate buffer (60:40 v/v) at pH 2.0±0.05 as the mobile phase at a flow rate of 0.8 mL/min and the detection was done at 248 nm was developed and fully validated for the determination of CRXA. The retention time of the drug was 3.693 min. The method produced linear responses in the concentration range of 0.45 to 80 µg.mL^{-1} of CRXA. The method was successfully validated in accordance to The International Conference on Harmonization (ICH) guidelines and was found to be reproducible for analysis of the drug in parental preparations [27].

New analytical method has been developed for the determination of cefuroxime in pharmaceutical formulations. The method involves the application of high performance Liquid chromatography (HPLC) for the quantitative analysis of cefuroxime. Chromatography was carried out on a C18 column (150 × 4.6 mm, 3 µm) with mobile phase comprises of 2.47× 10^{-4} M Octane 1-sulfonic acid sodium salt: acetonitrile (65:35). The mobile phase was maintained to flow at a rate of 0.5 mL/min and the measurements were made at 254 nm. HPLC method has a shorter analysis time of 10 min. The developed method obeyed the Beer's law in the range of 5- 300 µg.mL^{-1} [32].

In general, HPLC method is more accurate and acceptable. But the instrument is not available in all labs. So, the present work was undertaken with the aim to develop and validate an economic and rapid UV spectrophotometric method with high accuracy and precision. The method will be helpful for the routine estimation of cefuroxime axetil in pure form and in pharmaceutical formulations.

2. MATERIALS AND METHODS

2.1. Equipment and Materials

Spectrophotometric measurements were made in Spectro scan 80 DV UV-VIS spectrophotometer with 1 cm quartz cells. An ultrasonic processor model Power sonic 405 was used to sonicate the sample solutions. The diluter pipette model DIP-1 (Shimadzu), having 100 µL sample syringe and five continuously adjustable pipettes covering a volume range from 20 to 5000 µL (model Piptman P, GILSON). SARTORIUS TE64 electronic balance was used for weighing the samples.

Cefuroxime axetil (99.9%) was supplied by Covalent laboratories private limited (India), Linezolid was provided as a gift sample by Balsam Pharma, Al Hawash, Homs, Syria. Sulbactam was provided as a gift sample by Ibn Hayyan Pharmaceuticals, Homs, Syria. Metronidazole was provided as a gift sample by AARTI DRUGS LIMITED Mumbai, India. BTB (97%) of analytical grade, chloroform were from Sigma-Aldrich. Na_2CO_3 and methanol extra pure were from MERCK. All other solvents and reagents were analytical grade chemicals.

Tablet commercial formulations were used for the analysis of CRXA. The pharmaceutical formulations subjected to the analytical procedure were as the follows:

(1) Zednad tablets, Diamond Pharma, Damascus suburb, Syria, each tablet contains 250 mg of CRX (equivalent to 300.7 mg CRXA) (Mfg. 4/2018, Exp. 4/2021) and 500 mg of CRX (equivalent to 601.4 mg CRXA) (Mfg. 3/2018, Exp. 3/2021).

(2) Cefrocim tablets, Delta for medicaments, Aleppo, Syria, each tablet contains 250 mg of CRX (equivalent to 300.7 mg CRXA) (Mfg. 6/2016, Exp. 6/2019) and 500 mg of CRX (equivalent to 601.4 mg CRXA) (Mfg. 7/2016, Exp. 7/2019).

2.2 Standard stock solutions

1×10^{-3} mol.L^{-1} of pure CRXA was prepared in chloroform. This solution was prepared by good mixing 5.11 mg of CRXA with 0.10 g of Na_2CO_3, adding 0.30 mL methanol, and solved in 7 mL chloroform using ultrasonic for 15 min, filtered over a 10 mL flask and washed by the same solvent, then diluted to 10 mL with chloroform. The solution was stored in dark bottle and kept in the refrigerator for not more than a week. The stock solution was further diluted daily just before the use to obtain working solutions of CRXA in the concentration range 2.00-50.00 µM (1.021 – 25.524 µg.mL^{-1} of CRXA).

Stock standard solution of bromothymol blue (BTB) $1x10^{-2}$ mol.L^{-1}:

Accurately weighed 160.9 mg of bromothymol blue (BTB) was dissolved in chloroform into a volumetric flask (25 mL) and diluted up to mark with chloroform.

2.3 Recommended Procedure

Aliquots of 1×10^{-3} mol.L^{-1} CRXA solution (20, 50, 100, 150, 200, 300, 400 and 500 µL) containing: 2.00, 5.00, 10.00, 15.00, 20.00, 30.00, 40.00 and 50.00 µM (1.021, 2.552, 5.105, 7.657, 10.210, 15.314, 20.419 and 25.524 µg.mL^{-1}) of CRXA were transferred into a series of 10 mL calibrated volumetric flasks. Then 0.100 mL of BTB solution ($1x10^{-2}$ mol.L^{-1}) was added. The volume was made up to the mark with solvent and the absorbance was measured at λ_{max} 410 nm in chloroform, against a similar reagent blank.

2.4 Procedure for pharmaceutical formulations

Twenty tablets of each studied pharmaceutical formulation were weighed accurately, finely powdered and mixed well. An amount of the powder equivalent to the weight of tenth tablet was mixed well with 0.10 g of

Na_2CO_3, adding 0.30 mL methanol, and solved in 7 mL chloroform using ultrasonic for 15 min, filtered over a 25 mL flask and washed by the same solvent, then diluted to 25 mL with chloroform. This solution contains the follows: 1.0 and 2.0 $mg.mL^{-1}$ of CRX (i.e. 1.203 and 2.406 $mg.mL^{-1}$ of CRXA) for all studied pharmaceutical formulations contain 250 and 500 mg/tab, respectively.

Five solutions were prepared daily by diluting 0.100 mL from each stock solution of pharmaceuticals for contents: 250 or 500 mg/tab, then 0.100 ml from stock standard solution of BTB was added and adjusted the volume up to 10 mL with chloroform (these solutions contain 10 or 20 $\mu g.mL^{-1}$ of CRX respectively and $1x10^{-4}$ $mol.L^{-1}$ of BTB; test solutions).

3. RESULTS AND DISCUSSION

3.1 The effect of solvent

The effect of the solvents (acetonitrile, benzene, chloroform, dichloroethane, dichloromethane, ethylacetate and toluene) on absorbance of reagent (BTB), formed complex [CRXA]:[BTB] and the difference between them were studied. It was found that chloroform solvent was the best.

3.2 Absorption Spectra

UV-Vis spectra of CRXA, BTB and the formed complex CRXA:BTB solutions in chloroform was obtained. CRXA solutions do not absorb in the range 300-600 nm. BTB solutions have small absorption at λ_{max} 412 nm ($\varepsilon \approx 210$ L $.mol^{-1}.cm^{-1}$ in chloroform). [CRXA]:[BTB] complex solutions have maximum absorption at λ_{max} 410 nm in chloroform, ε for the complex was L mol^{-1} cm^{-1}, see Figure 1 as example.

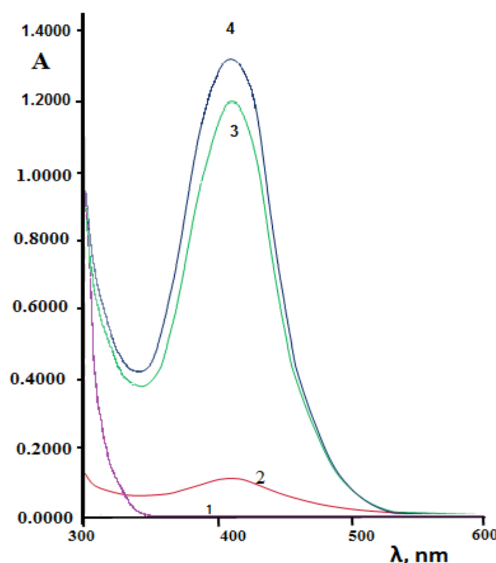


Fig.1. UV-Vis spectra in chloroform of: 1- $0.5x10^{-4}$ $mol.L^{-1}$ of CRXA; 2- $5.0x10^{-4}$ $mol.L^{-1}$ of BTB; 3- $0.5x10^{-4}$ $mol.L^{-1}$ ion-pair complex ($0.5x10^{-4}$ $mol.L^{-1}$ of CRXA with $5x10^{-4}$ $mol.L^{-1}$of BTB); Blank is $5.0x10^{-4}$ $mol.L^{-1}$ of BTB, 4- $0.5x10^{-4}$ $mol.L^{-1}$ ion-pair complex ($0.5x10^{-4}$ $mol.L^{-1}$ of CRXA with $5x10^{-4}$ $mol.L^{-1}$ of BTB); Blank is chloroform, ℓ =1 cm.

3.3 Optimization of Variables

The different experimental parameters affecting the spectrophotometric determination of CRXA through ion-pair complex [CRXA]:[BTB] formation with BTB in chloroform was studied in order to determine the optimal conditions for the determination of CRXA.

3.4 The effect of time and temperature

The effect of time and temperature on the complex [CRXA]:[BTB] formation was studied within the ranges 5-120 min and 15-45°C. It was found that the formed complex wasn't affected by time or temperature at those ranges.

3.5 The effect of BTB concentration

The effect of BTB concentration on complex [CRXA]:[BTB] formation was investigated. It was observed that the absorbance of the formed complex increased coinciding with increasing the ratio of C_{BTB}:C_{CRXA} until the ratio (2:1).

3.6 Stoichiometric Relationship

3.6.1 The molar ratio method

The composition of CRXA:BTB complex were determined by the molar ratio method and Job's method of continuous variation [40]. The stoichiometry of CRXA:BTB complex was studied by molar ratio method according to following equation: A_{max}=f([BTB]/[CRXA]) at λ_{max} 410 nm in chloroform. It confirmed that the binding ratio of CRXA:BTB complex is equal to (1:1); where the concentration of CRXA was constant (50 μM) and the concentrations of BTB changed from 0 to 200 μM, see Figure 2. The formation constant of the ion pair complex [CRXA]:[BTB] is $3.12x10^7$ in chloroform.

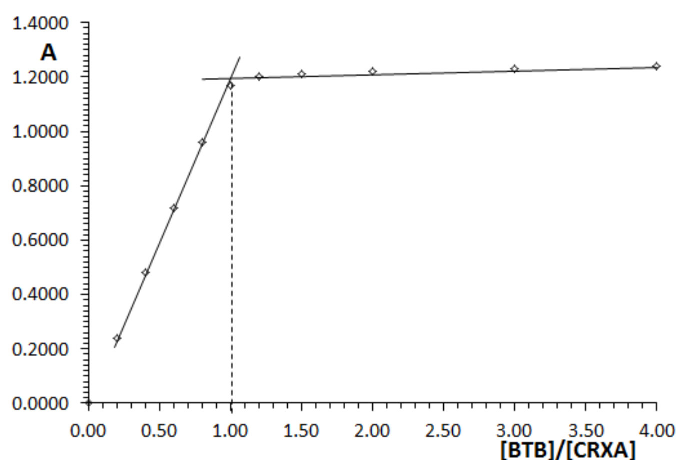


Fig.2. Molar ratio method to calculate binding ratio of CRXA:BTB complex at λ_{max} 410 nm in chloroform ([CRXA]=50 μM, blank is chloroform, ℓ =1 cm).

3.6.2 The Job's method

Continuous variation was utilized to check the composition of CRXA:BTB complex at λ_{max} 410 nm in chloroform. The absorbance of the complex in used solvent were plotted against the mole fraction [BTB]/([CRXA]+[BTB]), where [CRXA]+[BTB]=50 μM. The plot reached maximum value at a mole fraction of 0.5, see Figure 3. This indicated complex formation (CRXA:BTB) in the ratio of (1:1). The formation constant of the ion- pair complex [CRXA]:[BTB] is $3.5x10^7$.

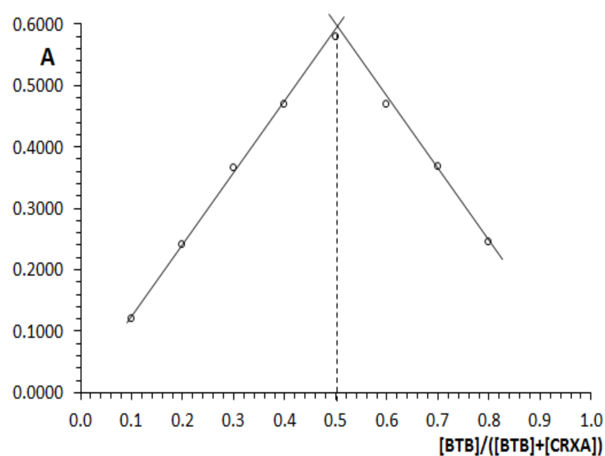
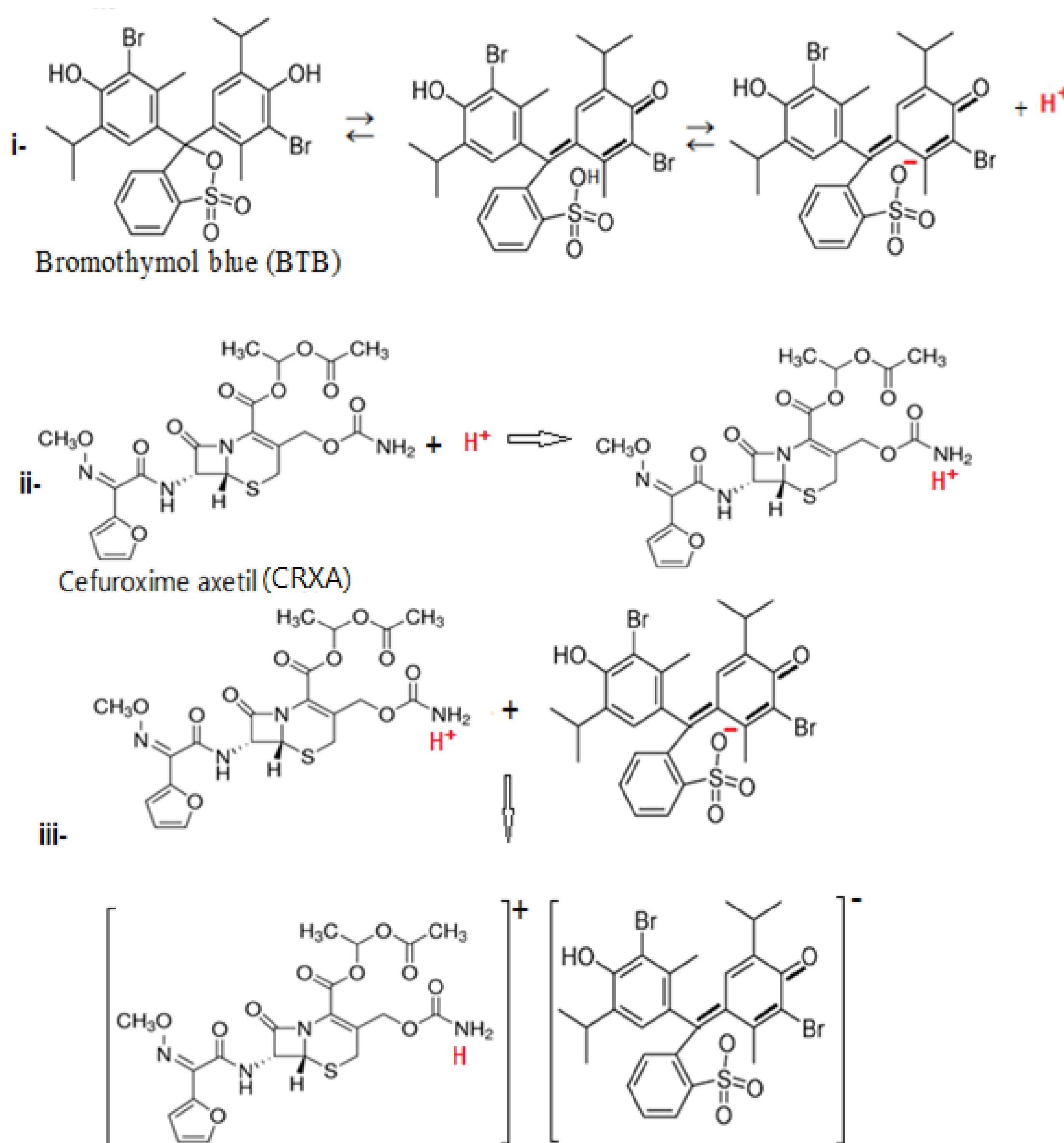


Fig.3. Job's method of continuous variation to calculate binding ratio of CRXA:BTB complex at λ_{max} 410 nm in chloroform ([CRXA]+[BTB]=50μM, blank is chloroform, ℓ =1 cm).

3.7 Mechanism of reaction

Anionic dyes such as BTB form ion-pair complexes with the positively charged nitrogen-containing molecule. The colour of such dyes is due to the opening of lactoid ring and subsequent formation of quinoid group (deprotonated). CRXA is reacted with the dye at pH<3.8; (in pH>5.4 and alkaline solution BTB gives blue

colour). Each drug-dye complex with two oppositely charged ions (positive on the drug and negative on the dye) behaves as a single unit held together by an electrostatic binding [41]. The suggested mechanism of CRXA-BTB ion-pair complex formation is shown in Scheme 3.



Scheme 3: The possible reaction mechanism of [CRXA]:[BTB] complex formation.

3.8 Calibration curve

The calibration curve of CRXA in pure form through complexation with BTB showed excellent linearity over concentration range of 2.00-50.00 µM (1.021-25.524 µg.mL^{-1}) in presence of 1.0×10^{-4} mol.L^{-1} of BTB with good correlation coefficient (R^2=0.9996) in chloroform. Regression equation at λ_{max} was as the follows: y=0.0241x+0.0039 in chloroform. Figures 4 showed the calibration curve of complex ([CRXA]:[BTB]) in presence of 1.0×10^{-4} M of BTB as example. The spectra characteristics of the method such as the molar absorptivity (ε) Beer's law, regression equation at λ_{max} (y=a.x+b); where y=absorbance, a=slope, x=concentration of CRXA by µM, b=intercept, the correlation coefficient, limit of detection (LOD) and limit of quantification (LOQ) and the optimum conditions for spectrophotometric determination of CRXA through ion-pair complex formation using BTB in chloroform is summarized in Table 1.

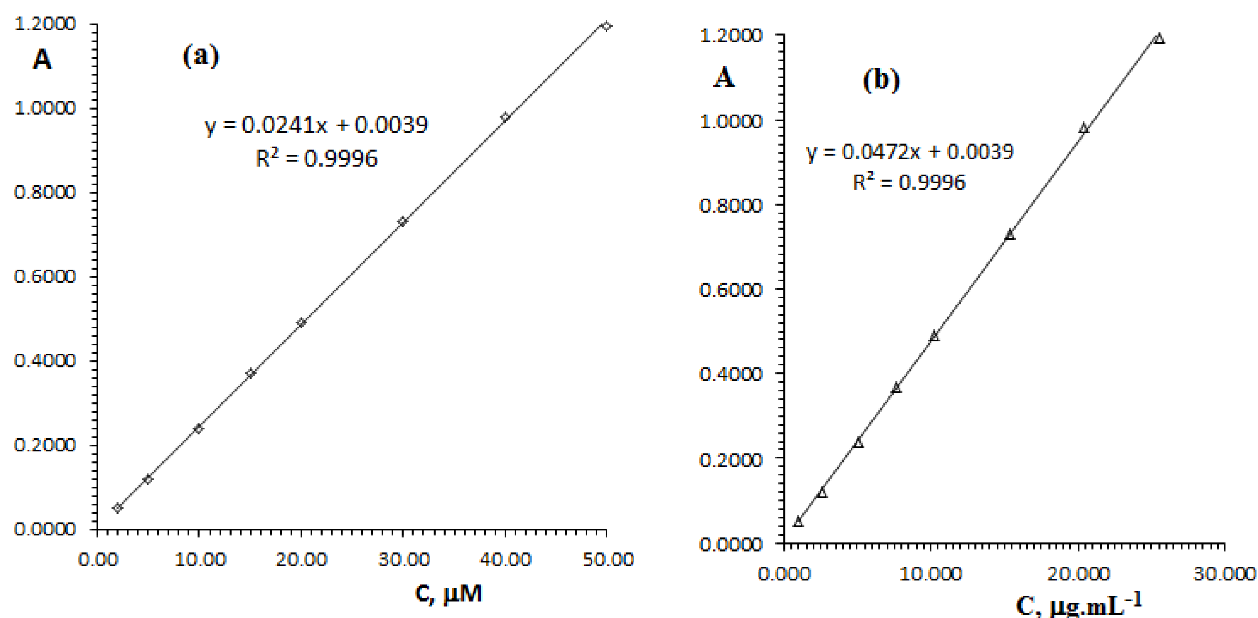


Fig 4: Calibration curve for determination of CRXA according to optimal conditions at λ_{max} 410 nm (in present of 1.0×10^{-4} M of BTB) where CRXA:2.00–50.00 µM {Blank is BTB solution in chloroform 1.0×10^{-4} M; ℓ = 1 cm; **a** by µM and **b** by $\mu g.mL^{-1}$ }.

Table 1. The parameters established for spectrophotometric determination of CRXA by complex formation with BTB in chloroform.

Parameters	**Operating values**
λ_{max} of CRXA: BTB complex, nm	410
Beer's Law Limit, for C_{CRXA} , µM	2.00-50.00
Beer's Law Limit, for C_{CRXA} , $\mu g.mL^{-1}$	1.021 – 25.524
Molar absorptivity of [CRXA]:[BTB] complex (ε) $L.mol^{-1}.cm^{-1}$	24000
Regression equation for [CRXA]:[BTB] by µM at λ_{max} =410 nm:	
Slope	0.0241
Intercept	0.0039
Correlation coefficient (R^2)	0.9996
LOD , $\mu g.mL^{-1}$	0.13
LOQ , $\mu g.mL^{-1}$	0.39
RSD%	4.2
C_{BTB}: C_{CRXA}, M	≥2
Stability	6 h
Temperature of solution	25±5°C

n=5, t=2.776.

4. Analytical results

Spectrophotometric determination of CRXA through complexation with BTB in chloroform within optimal conditions using calibration curve was applied. The results, summarized in Table 2, showed that the determined concentration of CRXA was rectilinear over the range of 2.00-50.00 µM (1.021–25.524 µg.mL^{-1}) , with relative standard deviation (RSD) not more than 4.2%. The results obtained from the developed method have been compared with the official HPLC method [27] and good agreement was observed between them.

Table 2: Spectrophotometric determination of CRXA through complex formation with BTB within optimal conditions using calibration curve in chloroform (n=5, t=2.776).

(Taken)		$\bar{X}$ ±SD, µg.mL^{-1} (Found)	$\bar{x} \pm \frac{t.SD}{\sqrt{n}}$, µg.mL^{-1}	RSD%	$\bar{X}$, µg.mL^{-1} HPLC [27]
X_i, µM	X_i, µg.mL^{-1}				
2.0	1.021	0.977±0.041	0.977± 0.051	4.2	1.094
5.0	2.552	2.460±0.096	2.460± 0.119	3.9	2.500
10.0	5.105	5.002±0.185	5.002± 0.230	3.7	5.082
15.0	7.657	7.756±0.279	7.756± 0.347	3.6	7.682
20.0	10.210	10.299±0.360	10.299± 0.447	3.5	10.346
30.0	15.314	15.383±0.523	15.383± 0.650	3.4	15.027
40.0	20.419	20.680±0.682	20.680± 0.847	3.3	20.580
50.0	25.524	25.235±0.782	25.235± 0.971	3.1	25.046

5. Applications

The developed spectrophotometric method was applied to determine CRXA in some pharmaceutical preparations through complex formation by BTB in chloroform according to the optimal conditions. The results of quantitative analysis for CRXA in pharmaceutical preparations were summarized in Table 3. The Proposed method was simple, direct, specific and successfully applied to the determination of CRXA in pharmaceuticals without any interference from excipients. Average recovery ranged between 99.6 to 101.3%. The results obtained by this method agree well with the contents stated on the labels and were validated by HPLC method [27].

6. METHOD VALIDATION

The developed method for simultaneous estimation of CRXA has been validated in accordance with the International Conference on Harmonization (ICH) guidelines [42].

6.1 Specificity

The specificity of the method was ascertained by analyzing standard CRXA in presence of excipients. There was no interference from the common excipients.

Table 3: Determination of CRX, in some Syrian pharmaceutical preparations using spectrophotometric method through complex formation with BTB in chloroform,

λ_{max} 410 nm, n=5, t=2.776).

Tablet dosage form	Label Claim of CRX, mg/tab.	*Mean ±SD (CRX), mg/tab.	RSD%	Assay %	Mean ±SD (CRX), mg/tab. by HPLC [27]	Assay %, by HPLC [27]
Zednad tablets	250	254±9.6	3.8	101.6	253±7.1	101.2
	500	498±15.9	3.2	99.6	499±9.8	99.8
Cefrocim tablets	250	242±9.8	3.7	96.8	243±7.2	97.2
	500	506±16.2	3.2	101.2	504±9.6	100.8

6.2 Linearity

Several aliquots of standard stock solution of CRXA were taken in different 10 mL volumetric flask in presence of 1.0×10^{-4} $mol.L^{-1}$ of BTB and diluted up to the mark with chloroform such that their final concentrations were 2.00-50.00 µM (1.021–25.524 $\mu g.mL^{-1}$) for CRXA. Absorbance was plotted against the corresponding concentrations to obtain the calibration graph, see Table 2. Linearity equations obtained were y=0.0241x+0.0039 (R^2=0.9996) for the mentioned range.

6.3 Precision and Accuracy

The precision and accuracy of proposed method was checked by recovery study by addition of standard drug solution to pre-analyzed sample solution at three different concentration levels (80%, 100% and 120%) within the range of linearity for CRXA. The basic concentration level of sample solution selected for spiking of the CRXA standard solution was 10.210 $\mu g.mL^{-1}$. The Proposed method was validated statistically and through recovery studies and was successfully applied for the determination of CRXA in pure and dosage forms with percent recoveries ranged from 99.6% to 101.3%, see Table 4.

Table 4: Results of recovery studies (n=5).

Level	Recovery%
80%	99.6
100%	99.4
120%	101.3

6.4 Repeatability

The repeatability was evaluated by performing 10 repeat measurements for 15.0 µM (7.657 µg.mL^{-1}) of CRXA using the studied method under the optimum conditions. The found amount of CRXA ($\bar{x}$ ± SD) 15.191±0.516 µM (7.756±0.264 µg.mL^{-1}) and the percentage recovery was found to be 101.3±3.4. These values indicate that the proposed method has high repeatability for CRXA analysis.

6.5 Robustness

The robustness of the method adopted is demonstrated by the constancy of the absorbance with the deliberated minor change in the experimental parameters such as the change in the concentration of excipients, C_{BTB} (10±5%), temperature (25±5°C), stability (6±0.5 h) and reaction time (5±1 min), see Table 5 which indicates the robustness of the proposed method. The absorbance was measured and assay was calculated for five times.

Table 5: Robustness of the proposed spectrophotometric method,

(n=5, t=2.776).

Experimental parameter variation	**Average recovery (%)**	
	C_{CRXA}	
	2.552 **µg.mL^{-1}**	15.314 **µg.mL^{-1}**
Temperature		
20°C	99.8	99.9
30°C	100.1	100.4
Stability		
5.5 h	99.7	99.9
6.5 h	100.1	100.3
Reaction time		
4.0 min	100.2	100.1
6.0 min	100.4	100.0

6.6 Sensitivity (LOD and LOQ)

The sensitivity of the method was evaluated by determining the LOD and LOQ. The values of LOD and LOQ for CRXA are 0.13 and 0.39 µg.mL^{-1}, respectively.

6.7 The homogenization of tablets

The homogenization of tablets in terms of the weight and the amount of drug was studied. We found that the mean weight and amount drug in the tablets was 0.7544 ± 0.0046 g (i.e. ±0.61%), 0.8577 ± 0.039 g (i.e. ±4.6%)

for Cefrocim tablets (250 and 500 mg/tab) and 0.4486 ± 0.0021g (i.e. ±0.47%) and 0.8577 ± 0.0046 g (i.e. ±0.54%) for Zednad tablets (250 and 500 mg/tab), respectively. While the mean amount drug in the tablets was 254±1.82 mg/tab (i.e. ±0.73%) and 497±21 mg/tab (i.e. ±4.2%) for Zednad tablets (250 and 500 mg/tab) and 244±6.98mg/tab (i.e. ±2.8%) and 505±5.2 mg/tab (i.e. ±1.03%) for Cefrocim tablets (250 and 500 mg/tab), respectively; which shows that homogeneity of tablets is good.

6.8 Interferences

The presence of 1:1 sulbactam or linesolid in the tablet interfere the determination of cefuroxime axetil (or cefuroxime) by 24% and 32% , respectively. While metronidazole can be considered as non-obstructive 1:1 (disability less than 5%) does not interferes.

7. CONCLUSION

The developed spectrophotometric method is simple, direct (extraction-free) and cost-effective for the determination of CRXA in pure and tablet dosage forms was applied. This method is based on formation of ion-pair complex between CRXA and BTB in chloroform ([CRXA]:[BTB]). Beer's law in the optimum experimental conditions using [CRXA]:[BTB] complex is valid within a concentration range of 1.021–25.524 $\mu g.mL^{-1}$. The developed method is applied for the determination of CRXA in pure and its commercial tablets without any interference from excipients with average assay of 96.8 to 101.6%. Associated drugs (sulbactam or linesolid) with cefuroxime are considered to be interfere, while metronidazole can be considered as non-interfere.

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