AMERICAN JOURNAL OF PHARMTECH RESEARCH

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Ecofriendly Analytical Methods To Estimate Cefixime in Bulk and Tablet Dosage form using Hydrotrophy

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ABSTRACT

Solubilization of poorly water-soluble drugs has been a very important issue in screening studies of new chemical entities as well as formulation research. Hydrotropy is one of the solubility enhancement methods for aqueous solubility of poorly water-soluble compounds. Cefixime HCl is poorly water soluble drug which shows good aqueous solubility in 2 M Sodium Benzoate solution. For quantitative estimation of Cefixime HCl in bulk and tablet dosage form, a titrimetric analytical method and spectrophotometric methods has been developed using 2 M Sodium Benzoate as a hydrotrope. Hydrotropic solution was employed to solubilize a practically water insoluble drug, Cefixime HCl in bulk and tablet dosage form to carry out titrimetric and spectrophotometric analysis precluding the use of organic solvents. The bulk containing Cefixime HCl was analyzed successfully. Statistical data proved accuracy, reproducibility and the precision of the proposed method. The presence of hydrotropic agent Sodium Benzoate did not interfere in the analysis. The proposed methods are new, simple, accurate, reproducible and eco-friendly.

Keywords: Cefixime HCl; Sodium Benzoate, Hydrotropy, Titrimetry, Spectrophotometry .

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Received 05 November 2012, Accepted 22 December 2012

Please cite this article in press as Patil VP *et al.*, Ecofriendly Analytical Methods To Estimate Cefixime in Bulk and Tablet Dosage form using Hydrotrophy. American Journal of PharmTech Research 2013.

INTRODUCTION

Hydrotropes are a class of chemical compounds that cause a several fold increase in the solubility for sparingly soluble solute under normal conditions. This phenomenon is termed as a hydrotropy. Various hydrotropic agents such as sodium benzoate, niacinamide, sodium salicylate, sodium acetate, sodium citrate and urea have been employed to enhance the aqueous solubility of large number of poorly water soluble drugs[1-3]. Drawbacks of organic solvents include higher cost, toxicity, pollution and error in analysis due to their volatility. Cefixime HCl has been studied and determined by relatively few procedures such as spectrophotometric[4-6], fluorimetric[7], high performance liquid chromatographic and high performance thin layer chromatographic[8] methods. Cefixime HCl forms a greenish colored product with Fehling solution[9]. In the present investigation, solution of 2M Sodium Benzoate (an economic hydrotropic agent) has been employed to solubilize a poorly water soluble drug, Cefixime HCl and its further titration was carried out with the help of Fehling's reagent as an indicator.

MATERIALS AND METHODS

Materials, chemicals and equipment

Analytical pure standard sample of Cefixime HCl was supplied as gift sample from Wockhardt Pharmaceuticals Ltd. (Aurangabad, India). Fehling's reagent used as a colouring agent and other reagents were purchased from S. D. Fine Chemicals Limited. A Standard Titrimetry Assembly and Shimadzu model 1800 digital spectrophotometer provided with 1 cm matched quartz cells was used for absorbance measurements.

METHOD DEVELOPMENT

Titrimetry Method

Analysis of Cefixime HCl in bulk sample by proposed titrimetric method:

In the proposed method, accurately weighed 0.1 g Cefixime HCl was solubilized in 20 ml of 2M Sodium benzoate solution in a 100 ml volumetric flask, dilute the mixture with distilled water upto the mark (stock A). To the 10 ml of stock A solution, add 5ml of Fehling's reagent as an indicator in 50ml volumetric flask, make up the volume with distilled water upto the mark (stock B). Take 10 ml stock B solution in conical flask and titrate it with 0.1 N HCl solutions till green colour vanishes completely. Perform a blank determination and make any necessary correction. Each ml of 0.1M hydrochloric acid is equivalent to 50.75 mg of $C_{16}H_{15}N_5O_7S_2 \bullet 3H_2O$.

Analysis of Cefixime HCl in tablet dosage form by proposed titrimetric method:

Weigh and powder 20 tablets of Cefixime HCl (ZIFI-100) Weigh accurately a quantity of the

powder equivalent to 100 mg of Cefixime HCl and transfer to 100 ml volumetric flask. Add 20 ml 2M Sodium Benzoate and shake properly for 10 min. to solubilize the drug and the volume was made up to the mark with distilled water (stock A). To the 10 ml of stock A solution, , add 5ml of Fehling's reagent as an indicator in 50ml volumetric flask, make up the volume with distilled water upto the mark (stock B). Take 10 ml stock B solution in conical flask and titrate it with 0.1N HCl solutions till green colour vanishes completely. Perform a blank determination and make any necessary correction. Each ml of 0.1M hydrochloric acid is equivalent to 50.75 mg of $C_{16}H_{15}N_5O_7S_2 \bullet 3H_2O$.

SPECTROPHOTOMETRIC ANALYTICAL METHOD

Preliminary solubility studies of Cefixime Hydrochloride:

Solubility of Cefixime HCl was determined in distilled water and hydrotropic solution of 2M sodium benzoate at 28°C ± 1°C. There was an enhancement in the solubility of drug in the hydrotropic solution, as compared with the solubility in distilled water.

Preparation of calibration curve of Cefixime Hydrochloride.

Accurately weighed 100 mg of Cefixime HCl and was solubilized by 20 ml of mixed hydrotropic solution of 2M Sodium benzoate, in a 100 ml volumetric flask and distilled water was added to make up the volume and was scanned in the uv-visible range at 800-200nm for the determination of λ max of Cefixime HCl by using blank solution. The λ max of Cefixime HCl was found to be 288 nm.

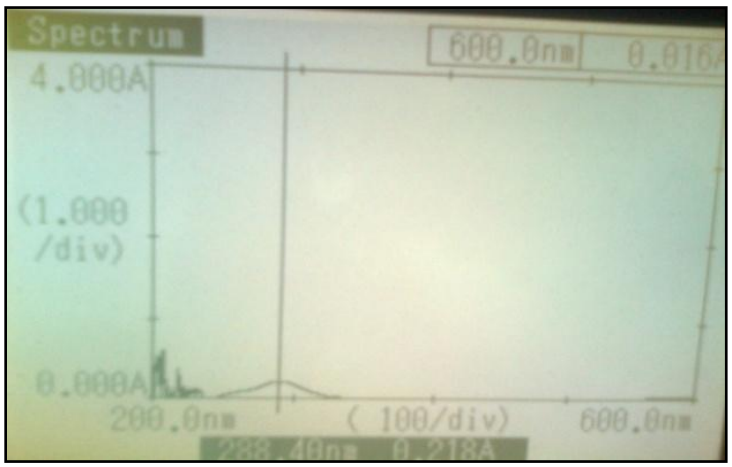

Figure.1: Spectrum of Cefixime HCl.

The stock solution(1000 µg/ml) was further diluted with distilled water to get various concentrations 0-25µg/ml of drug and their absorbance were noted at 288 nm against blank. A calibration curve was prepared by plotting the measured absorbance *versus* concentration (Figure.2).

Analysis of Cefixime Hydrochloride tablets by the proposed method:

Weigh and powder 20 tablets of Cefixime HCl. Weigh accurately a quantity of powder equivalent to about 100 mg of Cefixime HCl, add 20 ml of 2M Sodium benzoate, shake for 10 minutes and add sufficient water to produce 100 ml. Mix, filter and dilute 15 ml of filtrate to 100 ml with water. Measure the absorbance of the resulting solution at maximum about 288 nm. Calculate the content of Cefixime HCl as compare to the Cefixime HCl RS.

METHOD VALIDATION

Linearity, Detection and Quantification Limits:

A linear correlation was found between absorbance and concentration of Cefixime HCl (Fig.2).

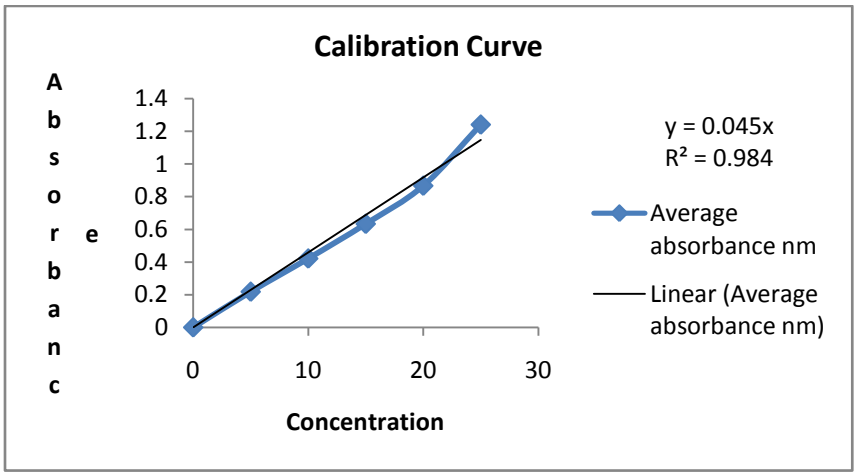

Figure. 2: Calibration curve for Cefixime HCl.

Regression analysis of Beer's law data using the method of least squares was made to evaluate the slope (b), intercept (a) and the correlation coefficient (r). The limits of detection (LOD) and quantification (LOQ), sensitivity parameters such as molar absorptivity and Sandell's sensitivity are also contained in Table 1.

Precision:

Precision was determined by studying the repeatability and intermediate precision. The coefficient of variance and standard error were calculated for the drug (Table 2).

Accuracy:

Accuracy was evaluated as percentage relative error between the measured concentrations and actual concentrations for Cefixime HCl (Bias %). The results obtained are compiled in Table 3 and show good accuracy for the method.

RESULT AND DISCUSSION

Titrimetric estimation of Cefixime HCl was carried out using Sodium benzoate hydrotrope and forms a coloured complex with Fehling's solution as a colouring agent. 20 ml of 2M Sodium

Benzoate and 5 ml of Fehling's solution were optimized. The method was validated for accuracy and precision as shown in Table 2 and Table 3.

Spectrophotometric estimation of Cefixime HCl was carried out using Sodium benzoate hydrotrope and evaluated at 288 nm. Validation parameters such as linearity, precision, accuracy and sensitivity (limit of quantitation and detection), were evaluated as shown in Table 1, Table 2 and Table 3.

Table 1: Optical characteristics data and validation parameters of Cefixime HCl.

Parameters	Analytical data
Linearity Range (µg/ml)	0-25
λ max	288 nm
ε, L/mol/cm	2.2491 x 10^3
Sandell sensitivity, µg/cm^2	0.2016
Slope (b)	0.045
Intercept (a)	0
Standard deviation about regression (Sy)	±0.0652
Standard deviation of Slope (Sb)	±0.002678
Standard deviation of intercept (Sa)	±0.0405
Correlation co-efficient (r)	0.9844
Limit of detection (LOD, µg/ml)	3.0513
Limit of quantification (LOQ, µg/ml)	9.2463

Table 2: Statistical Evaluation of Analysis of Cefixime HCl In Bulk And Tablet Sample by Titrimetric and Spectrometric Estimation.

Analyzed	% Drug Estimated		Coefficient of variation		Standard error	
	Titrimetry	Spectrometry	Titrimetry	Spectrometry	Titrimetry	Spectrometry
Bulk	98.78 ± 0.0808	99.88 ± 0.0808	0.808	0.908	0.4608	0.5608
Tablet	97.18 ± 0.5271	98.18 ± 0.6271	0.5271	0.7271	0.2961	0.4961

Table 3: Analysis Data of Cefixime HCl In Bulk And Tablet Sample.

Sr. no.	Amount of drug analyzed (mg)	Amount of Drug found (Titrimetric Estimation)(mg)		Percent Drug Estimated (Spectrometric Estimation) (%)	
		Bulk	Tablet	Bulk	Tablet
1	100	98.45	96.66	99.45	97.85
2	100	98.00	97.01	99.65	98.49
3	100	99.90	97.88	99.82	99.75

CONCLUSION

Hence, it is concluded that the proposed methods are new, simple, cost effective, accurate, safe and precise and can be successfully employed in the routine analysis of Cefixime HCl in bulk drug sample and Tablet Dosage Form. Advantage of these methods is that the organic solvent is not essential for the analysis of Cefixime HCl. There is a good scope for other poorly water-soluble drugs which may be tried to get solubilized in 2M sodium benzoate solution (as hydrotropic agent) to carry out their titrimetric and/or spectrophotometric analysis excluding the

use of costlier and unsafe organic solvents.

ACKNOWLEDGEMENT

The authors gratefully acknowledge the receipt of pure Cefixime HCl as gift sample from Wockhardt Pharmaceuticals Ltd. (Aurangabad, India). Authors express their gratitude to Yash Institute of Pharmacy, Aurangabad for providing the Instrumental and Chemicals facility.

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